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The SCREENING of WELL WOMEN for BREAST CANCER.

by

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This project was originated by, and carried out under the direction of Mr. Stanley Way, Director of the Department of Gynaecological Oncology. It was financed by the Women's Cancer Detection Society, Newcastle upon Tyne.

INTRODUCTION

One in twenty of all women in Britain may expect to develop cancer of the breast, and half of these will die from it (1). Lloyd Williams (2) stated in 1968 that the incidence of breast cancer in women of the Western world is increasing slightly every year. Cutler (3) states that there may be a slight increase, especially in younger women, in the United States of America, and Feinleib (4) states that since 1935 the incidence in women under fifty-five years has increased about forty-five percent, while above fifty-five the incidence is unaltered.

Although the results of treating most cancers have shown considerable improvement in recent years (5), the survival rates for breast cancer are no better now than in the days of Halstead (6, 7) - in spite of all the advances in surgery, anaesthesia, radiotherapy and pharmacology.

At the present time, the vast majority of breast cancers are discovered by the victim herself. The average size of the cancer at the time of initial treatment varies from 3.5 cm. according to Gershon-Cohen (8), to 5 cm. in a series published by Ross (9). Gershon-Cohen (8) and Lawson (10) point out that only thirty-five percent of all breast cancers are confined to the breast at time

of diagnosis.

Dunn (11), Donaldson (12), Forrest (7), Gershon-Cohen (13) and Strax (14) have published figures showing that, on average, the smaller the mass, the less the incidence of dissemination and so the better the prognosis. The supporters of the theory of biological pre-determinism (15, 16, 17) would deny this concept; this is a defeatist attitude especially as Gershon-Cohen (18), in studying the rate of growth of breast tumours, states that only thirty percent of tumours have short doubling times, growing and disseminating rapidly. While agreeing that tumour type and host response play a part in the end results, tumour size has been shown to be important. It would appear desirable to make a positive approach and attempt early diagnosis, rather than be resigned to the inevitable.

Much has been written (19) about self-palpation of the breast. Way's statement (20) that self-palpation is self-deception, has been supported by Gershon-Cohen (8), who announced that the campaign for self-examination, waged for the past twenty years by the American Cancer Society, had been a failure.

Gilbertson (21) has published his results for a group of women who had an annual clinical examination by a medical team; in the group of almost eight thousand women, sixty-six percent of the fifty five breast cancers which occurred, were found by the team, before recognition of the tumour's existence by the patient - all of whom had been instructed in self-palpation.

It has been estimated (10) that even in an organ as accessible as a breast it is seldom possible to palpate a tumour smaller than 1 cm. and in the fat breast, not even that. While this may be termed early by some standards, from the biological point of view, a palpable cancer is a late cancer (22). Collins (23) has stated that a breast cancer is clinically apparent for only the last quarter of its natural history.

AIM OF THE PROJECT

This survey is an attempt to diagnose breast cancer in a pre-clinical stage - before there is a palpable mass.

METHODS EMPLOYED

1. History
2. Clinical examination
3. Cytology of nipple discharge, if relevant
4. Thermography
5. Mammography

(1) History of the Patient

A specimen of the History Sheet, designed by me for this project, is shown overleaf.

(2) Clinical Examination

This is commenced with the patient seated in a good light and facing the examiner, also seated. Note is taken of the general size, shape and the contour of the breasts and nipples. Particular care is taken to exclude the presence of skin dimpling or early nipple retraction, both of which may be more easily demonstrated by altering the position of the breasts, e.g., by raising arms in the case of skin dimpling; bending forward should cause the nipples to fall away equally if they are free. The position of any scars is marked on a chart, as are any prominent superficial markings. The nipple area and each quadrant of the breast are palpated systematically between the finger

4, a.

Name .....

Address.....

.....

.....

Date of birth.....

Maiden name.....

No. of children.....

Age of youngest.....

Age of oldest.....

Breast feeding

No. of children.....

Duration of longest.....

Contraceptive Pill Yes/No

Specify:.....

How long.....

At present.....

or date stopped.....

Other hormones

.....

L.M.P. .....

Menopause date.....

Vaginal Cytology Yes/No

When..... Where .....

Breast Symptoms

.....

.....

Date of Examination.....

Film/camera No.....

Age.....

Family Doctor.....

Patients occupation.....

Husband's occupation.....

M. S. W. Sep. D.

Age at marriage.....

Married times.....

Family history of breast cancer.....

.....

.....

.....

.....

.....

Family history of other cancers.....

.....

.....

.....

.....

Previous operations on breast.....

.....

.....

.....

.....

and thumb, followed by palpation of the axilla. Then, standing behind the seated woman, the breasts are again palpated, against the chest wall, with the flat of the fingers; finally, from behind, the supra and inferior clavicular areas are examined.

(3) Nipple Discharge

When a nipple discharge is found during examination, a specimen is taken for cytological examination, as follows:-

Slides with a ground glass end, for labelling, are used. A film of the discharge is made and immediately placed in fixative (50 : 50 ether and ninety-five percent alcohol). This film is processed by the method of Papanicolaou.

(4) Thermography

Theory and development of Thermography

A thermogram is a pictorial representation of infra-red radiation. It depends upon the Stefan-Boltzman Law, which states that the quantity of infra-red emitted by a surface varies directly with the fourth power of the absolute temperature and with the emissivity of the surface. Every object, in maintaining thermal

equilibrium, is constantly either absorbing or emitting radiant energy.

Although the infra-red portion of the electro-magnetic scale was discovered by Sir William Herschel in 1800 and a method of imaging it was described by his son, Sir John, two years' later, it has not been put to practical use until about thirty to forty years' ago.

During the years 1934 to 1936, Hardy (24, 25, 26) reported a series of experiments showing that human skin, irrespective of its colour, was in the thermal sense, almost a perfect black body radiator, i.e., that it was a good absorber and a good emitter. He suggested that radiation techniques could have clinical potential. These experiments have been repeated more recently (1963) by Lloyd Williams (27) and his team. They showed that:-

(a) human skin emitted infra-red of wavelength two to twenty microns, with a maximum at 9.7 microns (ref. Planck's Law)

(b) that beyond six microns, skin does behave like a black body, i.e., absorption and emission are one hundred percent

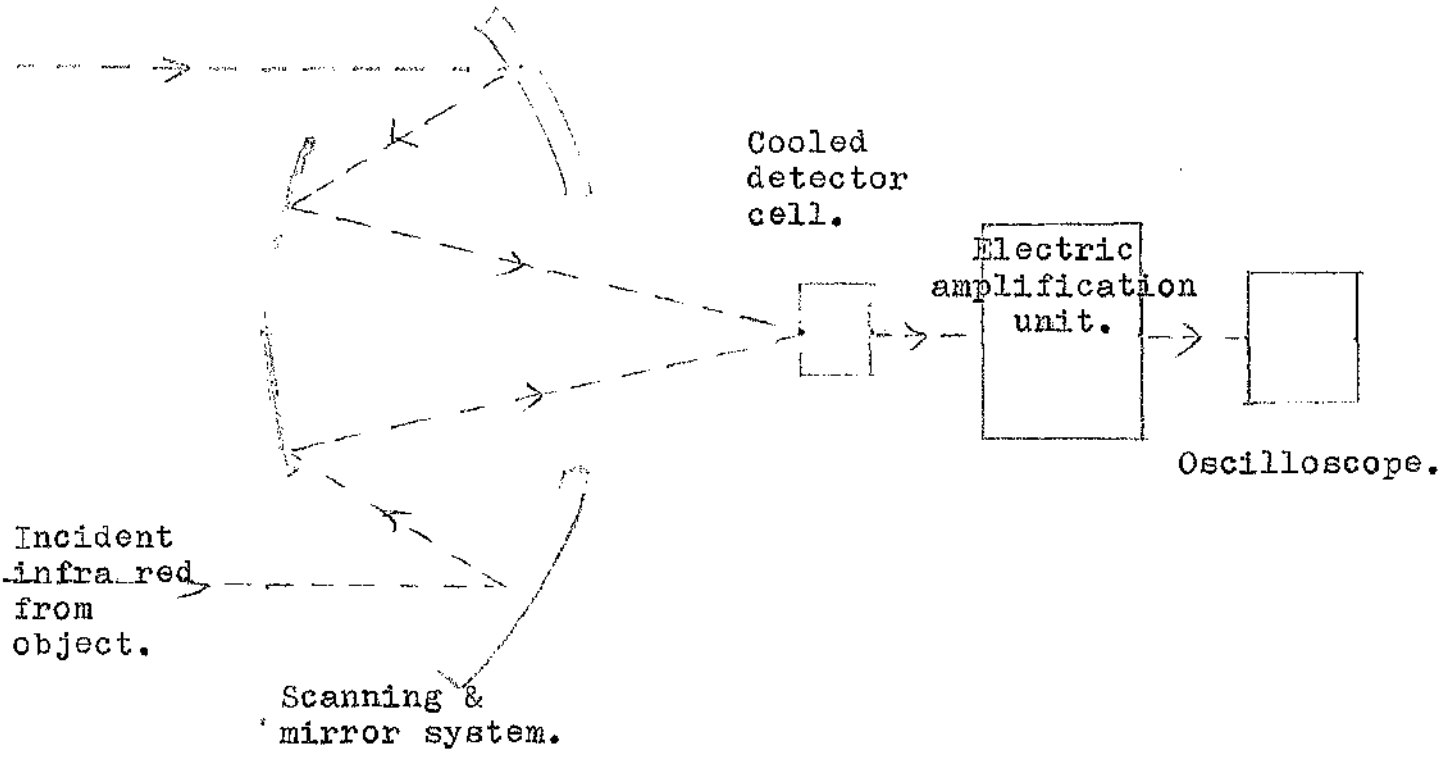
(c) that between three and six microns, skin emits slightly under one hundred percent, probably due to the water content of the epidermis, and

(d) that below three microns, the skin is by no means an efficient emitter and absorber, and in fact starts reflecting infra-red, a fact made use of in infra-red photography.

The great stimulus to research was for military purposes and was concentrated in the temperature range 600 - 1000°C associated with rocketry, guided missiles etc., - the infra-red radiation from, for example, a missile at 1000°C is of wavelength 2.3 microns. (ref. Wein's Law)

Thermographic techniques were developed whereby infra-red radiation is collected by an optical scanning device, converted into an electrical signal by a detector cell, amplified and displayed on a cathode ray tube. In this manner, invisible heat radiation is translated into something that can be seen and interpreted by the human eye, and also photographed.

FIGURE NO. 1



Diagramatic plan of thermovision.

The military implications, with high temperatures of the emitting surfaces, required detector cells most sensitive in the range 1 - 6 microns (Wein's Law) and indium antimonide fulfilled this need. It will be obvious that a detector cell of this limited sensitivity is not ideal for clinical use when skin has maximum radiation at 9.7 microns. Physicists are experimenting at present to find a new detector cell. Cadmium mercury telluride with a peak spectral response in the range 9 to 14 microns is a possibility

for the future but the ability to detect infra-red emission of longer wavelength may be out-weighed by the problems of increased background radiation. A preliminary report by Leftwich (28) would indicate that cadmium mercury telluride has no advantages over indium antimonide when scanning at room temperature: also a detector cell of cadium mercury telluride requires germanium optics which greatly increase the cost of the equipment.

The detector cell is cooled by liquid nitrogen, cooling of the detector enabling it to respond to smaller temperature changes much faster.

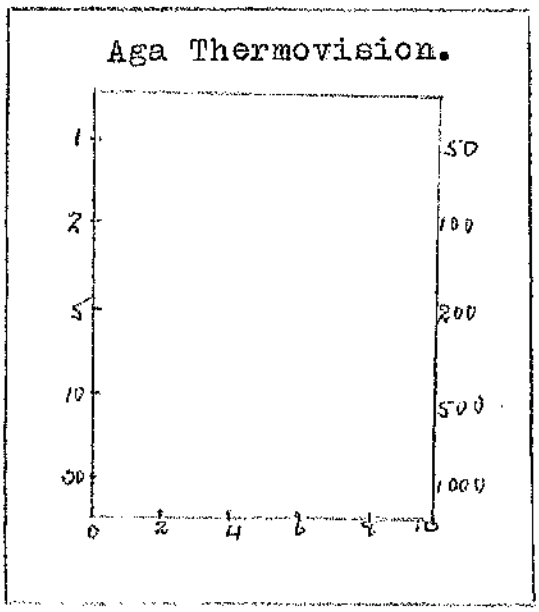
Lawson (10, 29), Barnes (30) and Cade (31) were early pioneers who developed instruments for medical thermography, after technical details came off the Secrets List in the late 1940's. Progress has been slow because of lack of an ideal detector, poor resolution, inadequate sensitivities, and slow speed of scan, varying from 1 frame/5 sec. to 30 frames/1 sec. Even now, it is largely a choice of good resolution and slow scan or poor resolution and rapid scan.

The Aga Thermovision, used in this survey, is a compromise of moderate resolution with a hundred lines per frame and about a hundred elements per line and a scan speed of sixteen frames per second.

I consider that a slower speed of scan is impractical for a screening procedure because it is difficult for the patient to remain motionless during a scan lasting more than a minute. A slow scan also increases the strain on the observer's eye when doing sessions of two to two and a half hours and would be very time consuming.

The oscilloscope screen is illustrated in Figure 2.

Figure 2



The ordinate is a scale from one to one thousand. This is the choice of sensitivity, the right hand high scale being purely for industrial use.

In this survey, I use sensitivities five, ten and twenty. The abscissa is a temperature scale, one to ten. With sensitivity,

e.g., ten, then each division on the temperature scale represents one degree. This temperature is relative, Wallace and Dodd (32) having shown that absolute temperatures were unnecessary in medical thermography. It is a question of comparing, one area with another.

With most up-to-date infra-red scanners, there is a choice of polarity, i.e., the operator may elect to have the hot end of the scale shown as black or as white. It is an established principle (32) of visual physiology that the human eye is capable of perceiving a greater number of shades of grey at the dark end of the scale when a light background is used and so it might appear better to use polarity of black as hot.

However, the display unit on the Aga Thermovision has isothermal controls which enable accurate temperature comparisons. They superimpose on the black and white picture a signal so that all surfaces with the same temperature appear as saturated white. In my opinion, this makes it preferable to use polarity of white as hot on the oscilloscope. Then my photographs, which are negatives, give hot as black - so fulfilling the ideal physiological conditions.

The Aga Thermovision can be fitted with a polaroid camera or a 35 mm. camera. In the early days of this survey, a polaroid camera was used. Very quickly this changed to a 35 mm. camera for the following reasons:-

(1) With 35 mm. film, the tonal range of black to white was more detailed

(2) it saved time during a screening session, as the film was developed later by a technician

(3) and it was much cheaper, working out at two pence per picture

Clinical Application of Thermography to Breast Screening

The application of thermography to breast conditions is based on the findings of Lawson published in 1956 (33). He demonstrated that the temperature of a breast cancer is greater than that of its surroundings and that the venous blood leaving a cancer is hotter than its arterial supply. This temperature gradient is considered to be due to:-

(a) an increased metabolic activity in the tumour with a build-up of deoxyribonucleic acid and ribonucleic acid releasing energy

(b) there is an increased blood and lymph supply to a cancer

(c) Lawson (34) also noted that the veins near a cancer had a deficiency in their muscle component and little vascular control, so they tended to dilate

(d) Gershon-Cohen (35) has suggested that enzyme activity at the periphery of a tumour may cause a rise in temperature, and also

(e) that the high glycolytic activity of tumours, described by Shrivastava and Quastel (36) may play a part

Thermography does not detect cancer, per se, but rather its biological effects and the host response to it.

To get the best results, thermography must be done in a room from which direct sunlight, air movements and draughts are excluded, and in a stable temperature of 18-20^{o}C.

The factors involved in heat loss from the skin are infra-red radiation, evaporation of sweat and convection in the following proportion according to Samuel (37) - forty-five percent radiation, twenty-five percent evaporation and thirty percent convection; no sweating occurs in an ambient temperature below 30^{o}C and exclusion of air currents reduces convection to a minimum.

The subject to be examined is allowed to cool, with the skin exposed for fifteen minutes, in a low ambient of 18-20°C. She is instfucted to sit with her arms akimbo to allow free cooling of the breast area (as per Plate 1).

Lloyd Williams (38) showed that when the unclothed body is exposed to lower temperature, the cooling rate is at first rapid, the maximum cooling effect of approximately 3°C occurring in the first fifteen minutes. Although equilibrium may not be achieved for one and a half hours, the normal skin temperature dropped on average by only a further 0.8°C after the first fifteen minutes, For practical purposes, cooling for fifteen minutes is sufficient.

The cooling period is essential as it has been shown (38) that the area of a cancer does not cool as does normal tissue, so the differential is increased. I have found that it is possible to obscure a hot spot by allowing the patient to warm up.

In the Well Women Clinic, the thermographic unit, consisting of ten changing and cooling cubicles and the thermovision room, is strictly temperature controlled. I have found it much more difficult to reduce the temperature in the summer months, than to

Plate 1.

This is a photograph of the instruction, exhibited in each cooling cubicle.

keep it stable by warming in winter.

For the purpose of this survey the detector cell in the Aga Thermovision was calibrated to be most efficient in the 18-22^{o}C range.

The interpretation of breast thermograms is greatly influenced by the vascular pattern of the breast. Anson and Wright (39) showed that the arterial supply to the breast approaches from two main sources, the internal mammary and lateral thoracic arteries, with a minor supply from the third, fourth and fifth intercostal arteries.

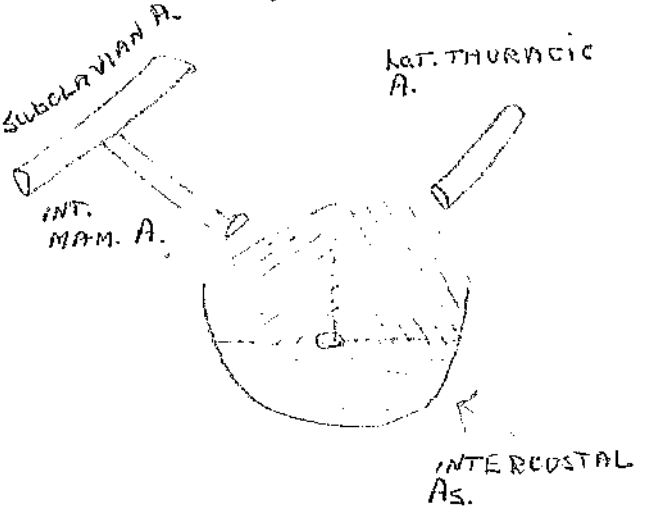


FIGURE NO. 3
Blood Supply to left breast

There is a circular peri-areolar plexus formed by branches from all three sources - also supplied from a deeper plexus. Cutler (40) comments on the fact that no main arterial supply reaches the breast in the inferior half. The venous drainage largely follows the arterial supply. I have found, however, that five percent of women have a prominent vein in the lower inner quadrant.

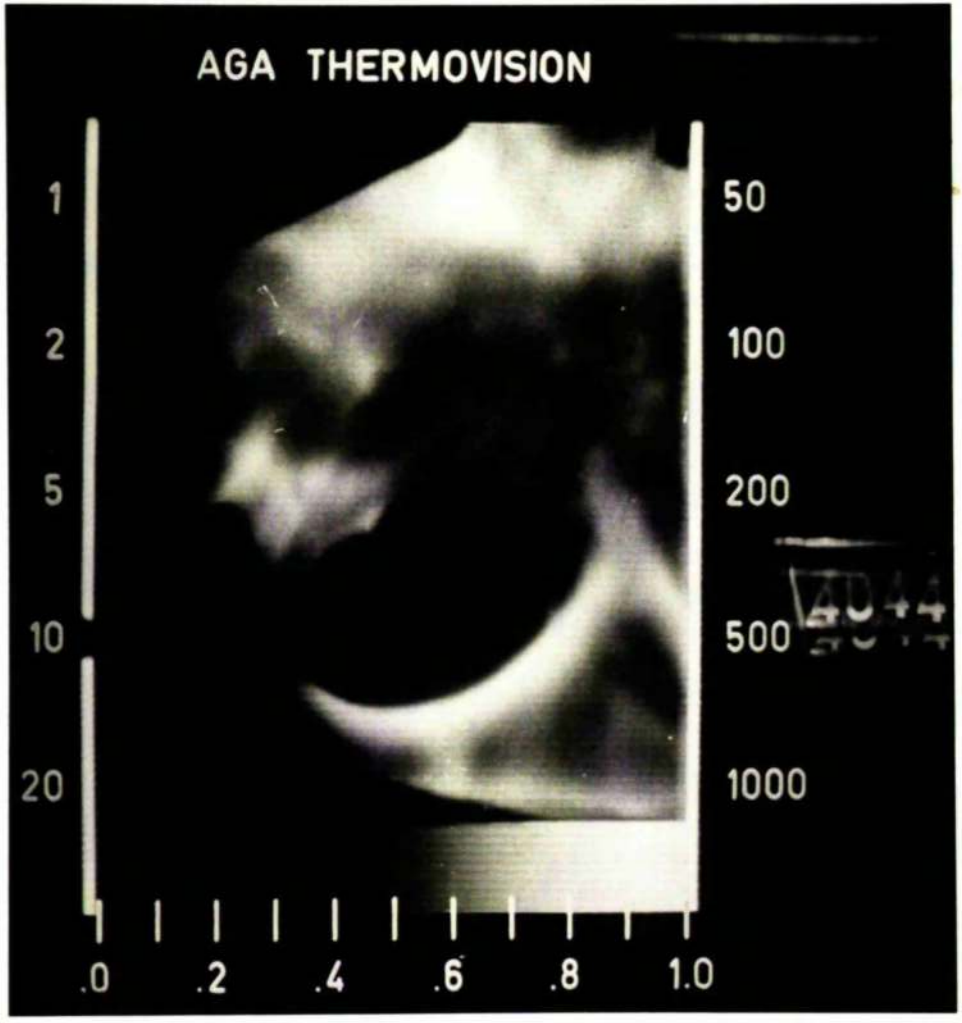
Using infra-red photography, Massopust and Gardner (41) showed that there are two main patterns of venous drainage - either a transverse pattern or a longitudinal pattern with a possible peri-areolar plexus, (The Circle of Haller). I have found that the longitudinal pattern is markedly more common.

In normal breasts, perfect symmetry of venous pattern is rare according to Harris and Greening (42), but the work done by Massopust and Gardner in 1950 (41) and more recently by Jones and Draper (43), indicates that the pattern is usually similar with no unilateral enlargement of veins.

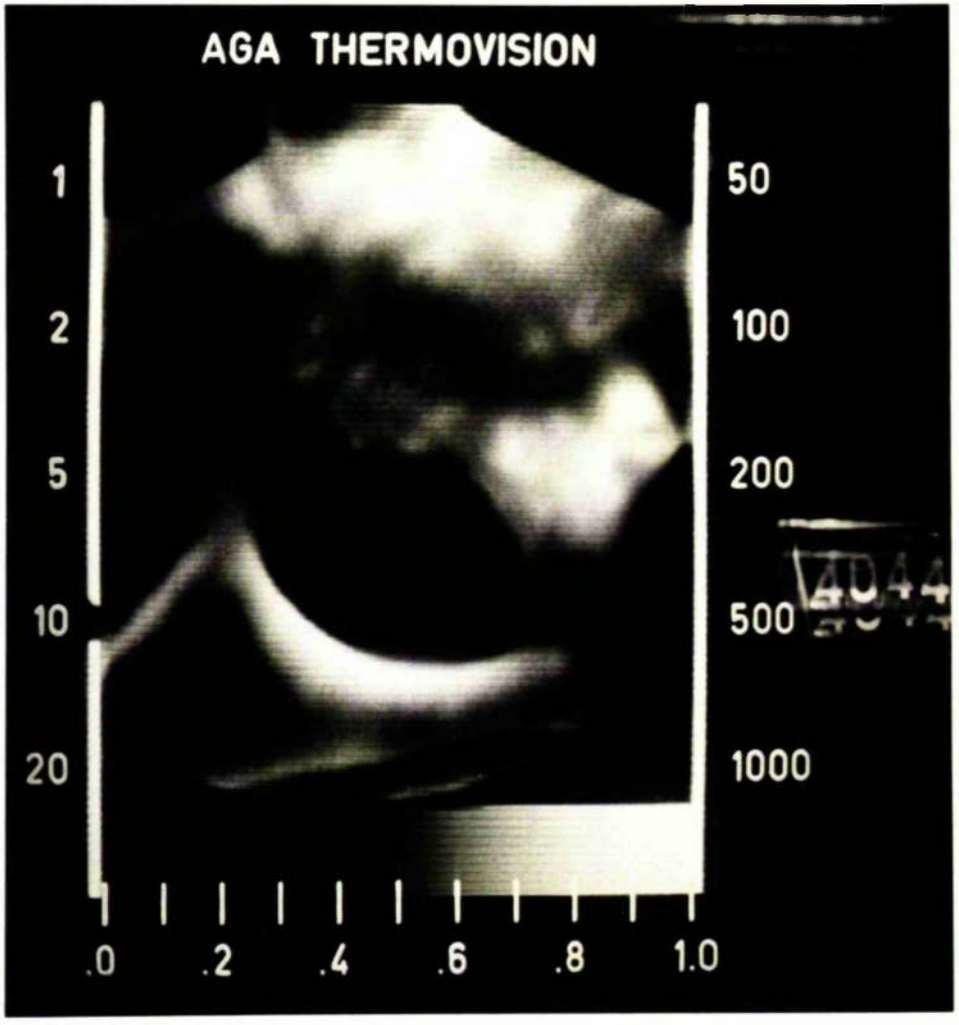
There are three basic types of breast thermogram - the avascular (Plate II), the vascular, of greater or lesser extent (Plate III), and thirdly, the mottled pattern (Plate IV).

Plate 11.

Right oblique.



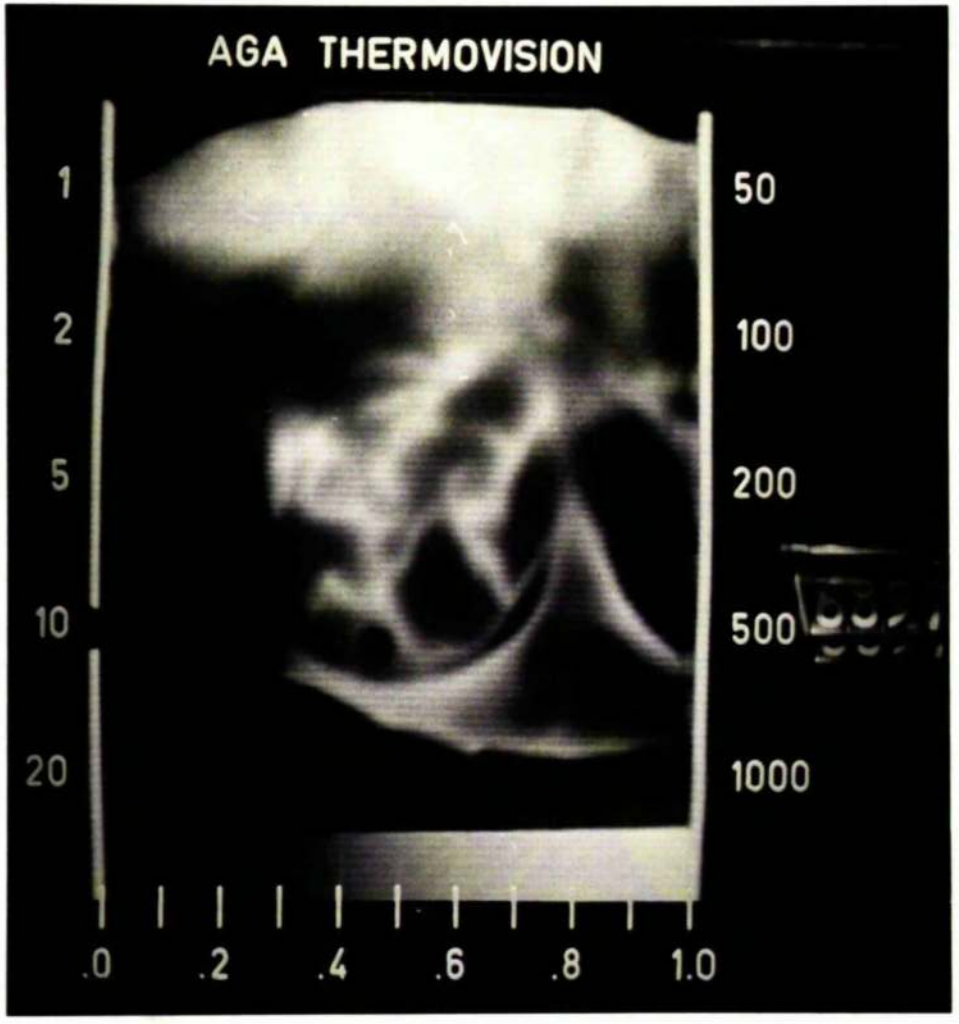
Left oblique.



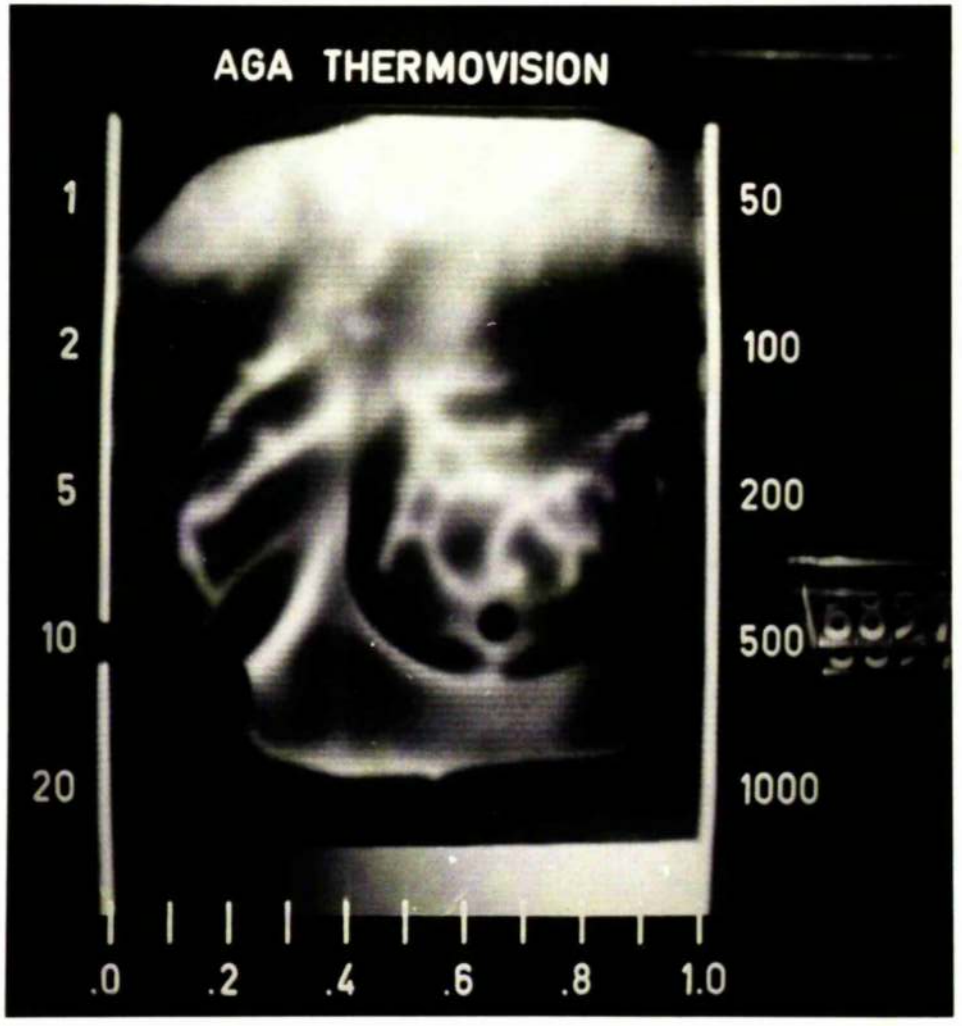
Normal Thermogram.- Avascular pattern.

Plate 111.

Right oblique.



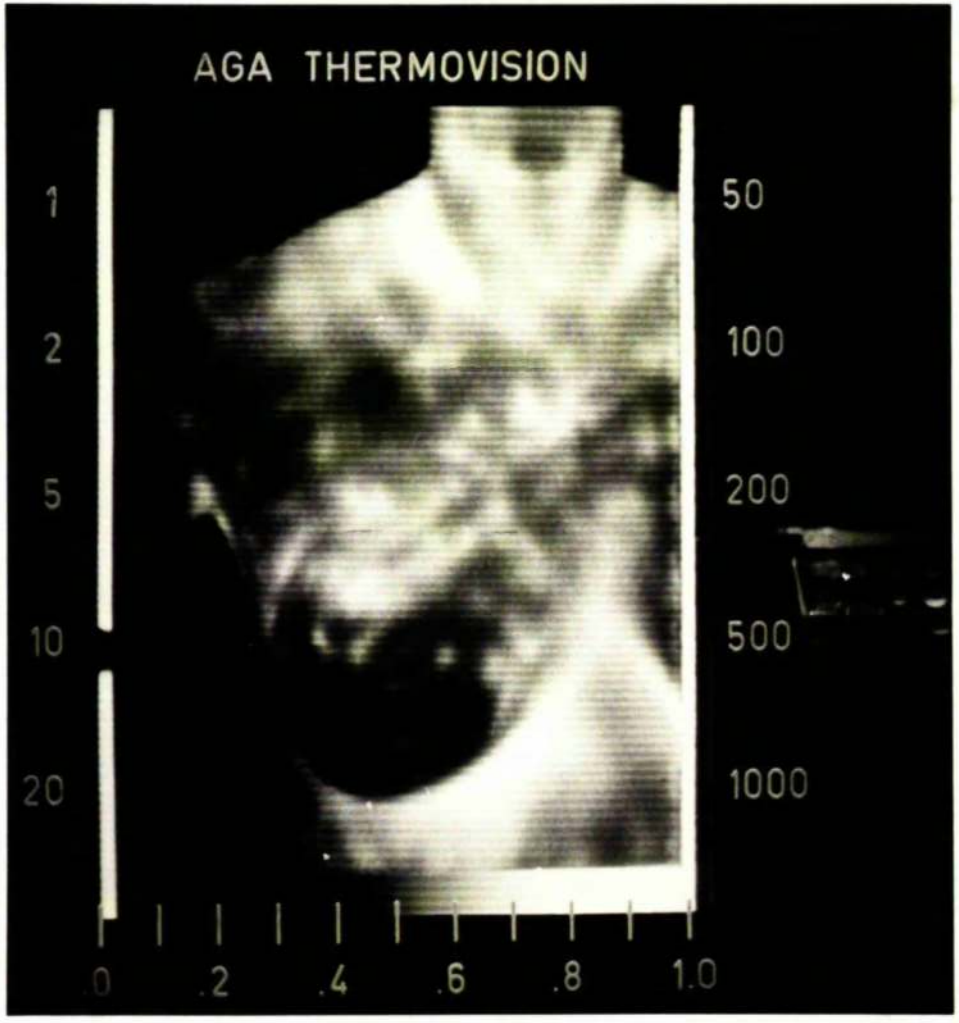
Left oblique.



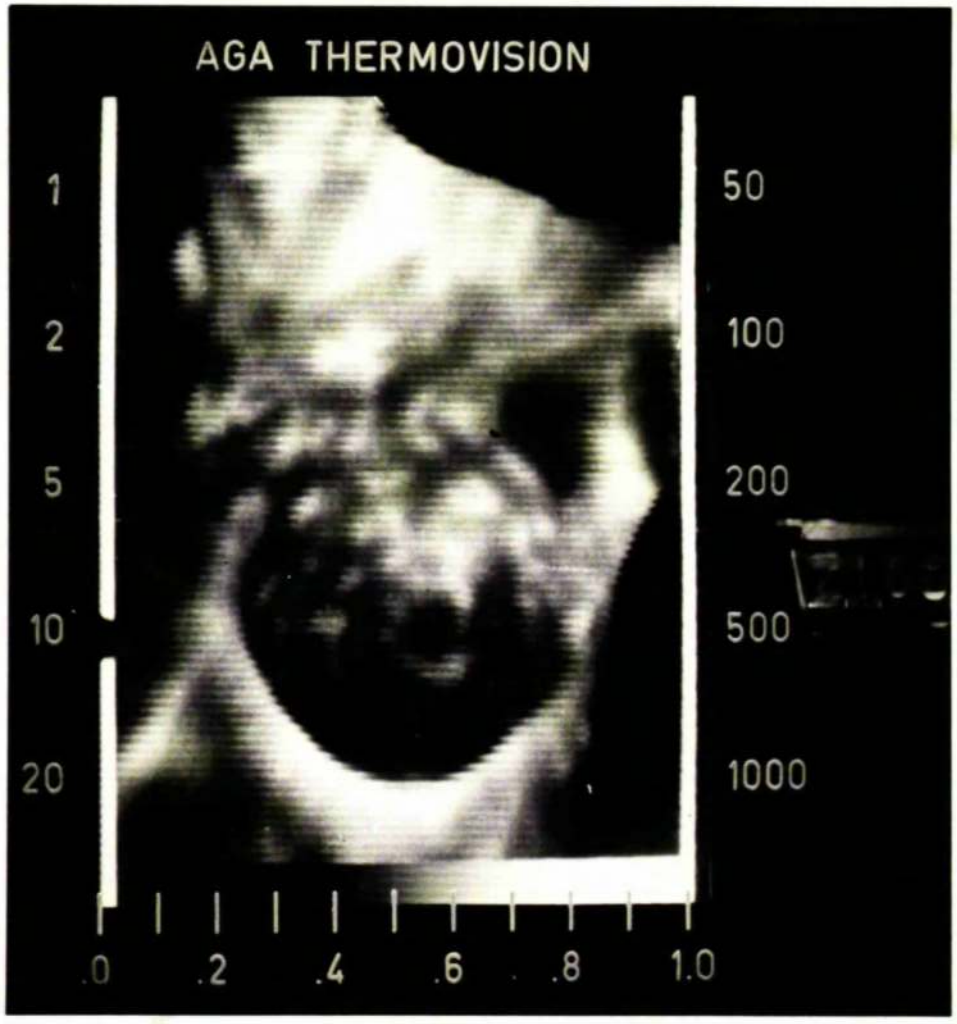
Normal thermogram.- Vascular pattern.

Plate 1V.

Right oblique.



Left oblique.



Normal thermogram.- Mottled pattern.

While I was learning the technique of thermography and to interpret thermograms, infra-red photography was used to correlate the thermographic picture with the venous pattern. In infra-red photography it is reflected, not emitted, infra-red radiation which is utilised. It is known that infra-red rays of wavelength 0.7 to 0.9 microns penetrate the skin to a depth of about 2.5 mm. and that blood absorbs this radiation more than surrounding tissue (25). It is this reflected radiation which is then photographed. To eliminate visible light, the camera lens was covered with a filter which absorbed radiation below 0.72 microns.

The thermographic features suggesting malignancy are:

(1) a localised area of increased heat emission or "hot spot" (Plate V)

(2) localised increased vascularity with more numerous or dilated vessels (Plate VI)

(3) a generalised increase in temperature (Plate VII)

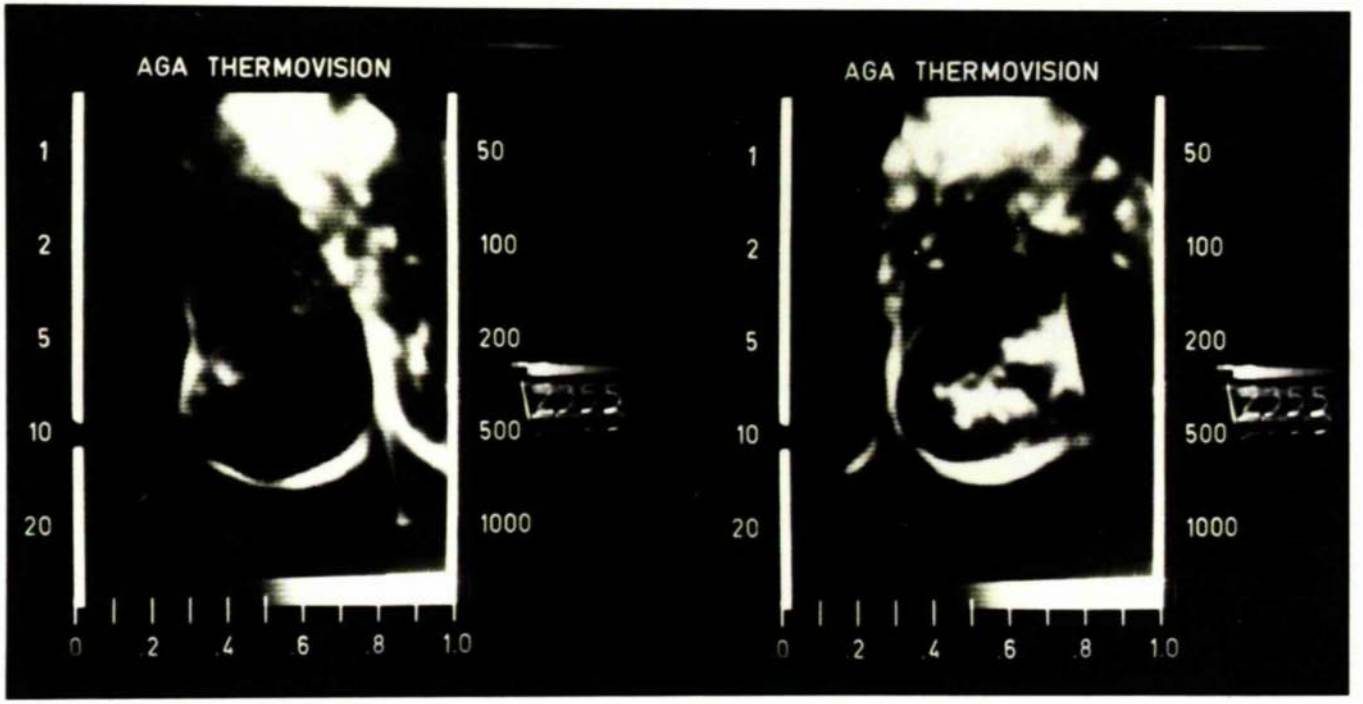
(4) increased heat of areolar area (Plate VIII)

The essential element is comparison of opposite parts, as well as an overall impression of the heat pattern, using one breast as a control for the other.

Plate V.

Right oblique.

Left oblique.

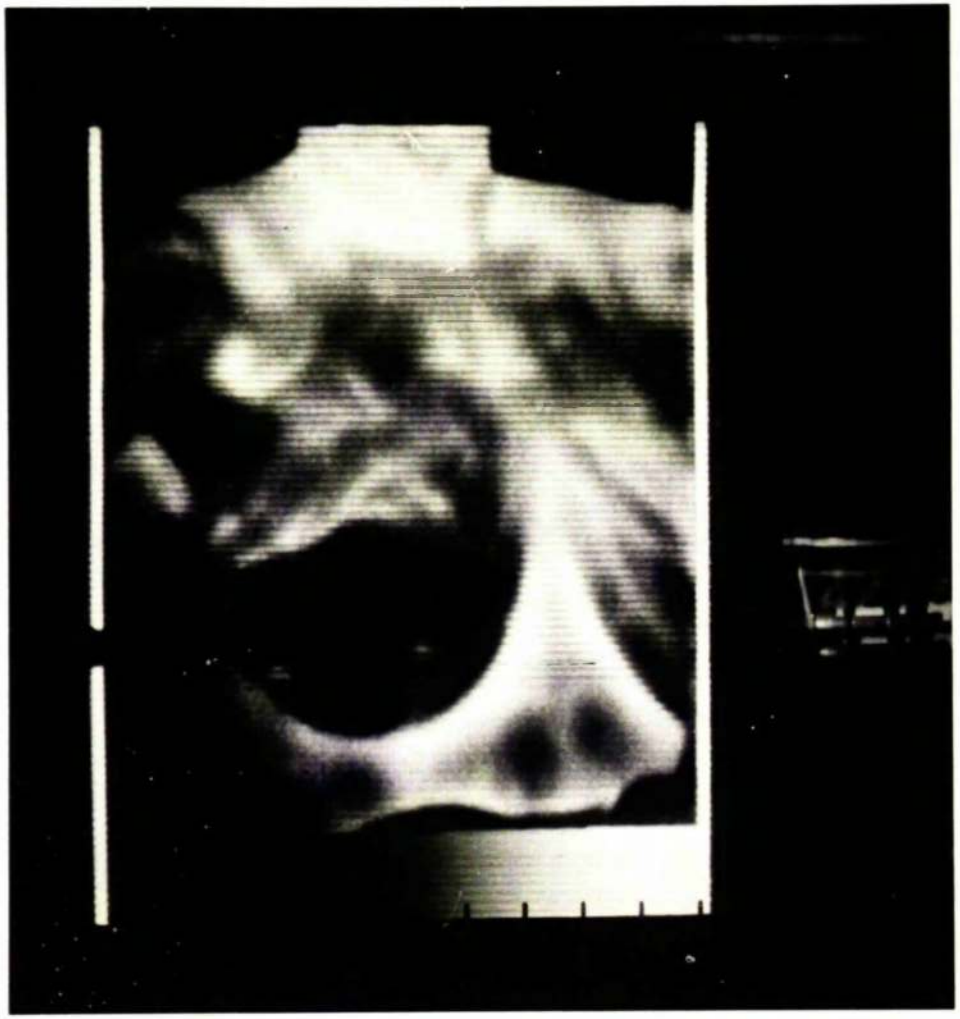


Abnormal thermogram. - hot spot in left breast. Histology cancer.

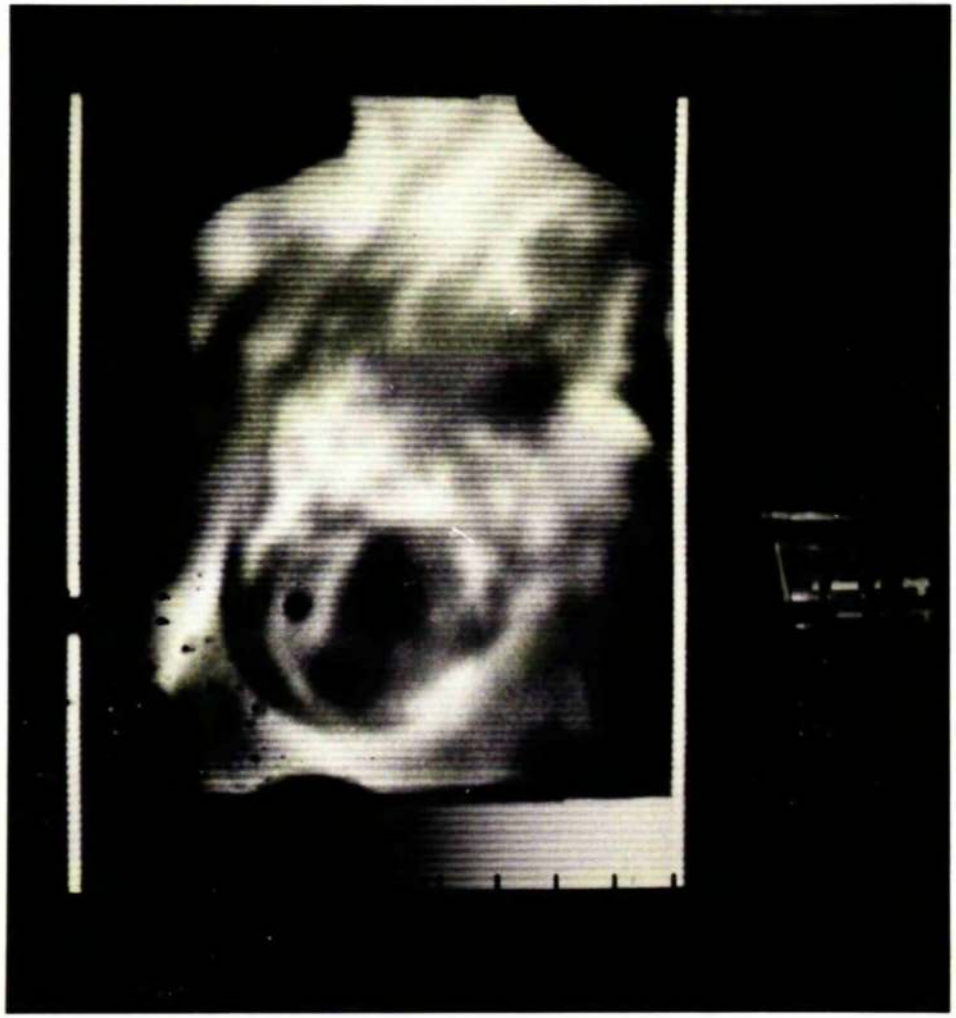
18,a.

Plate V1.

Right oblique.



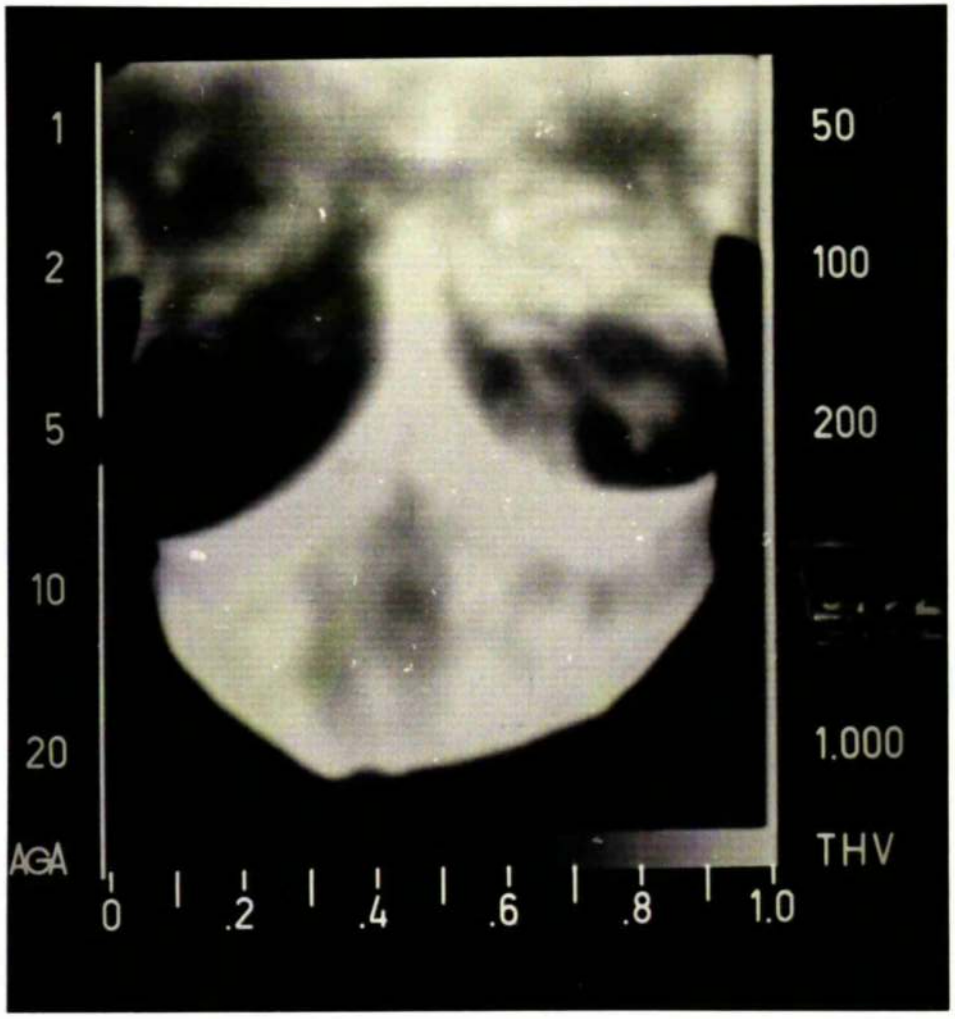
Left oblique.



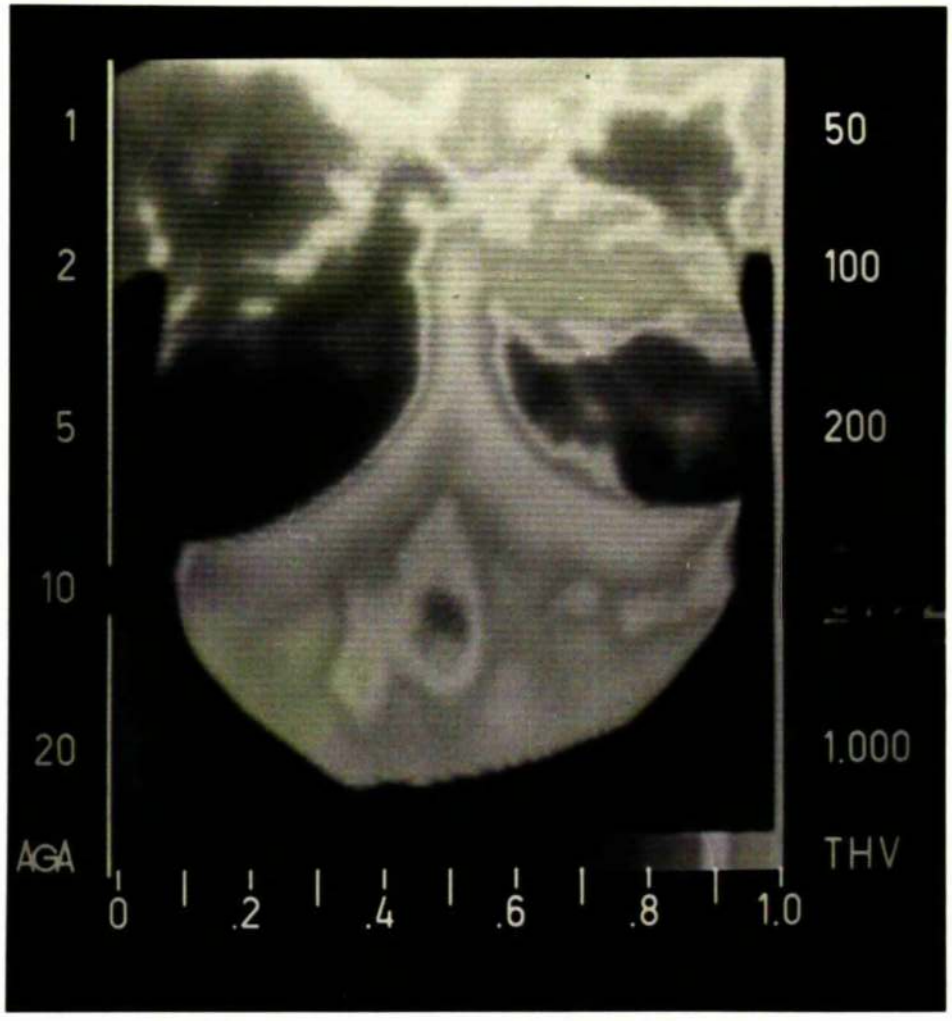
Abnormal thermogram. - localised increased vascularity in left breast. Histology cancer.

Plate V11.

a). Frontal view.



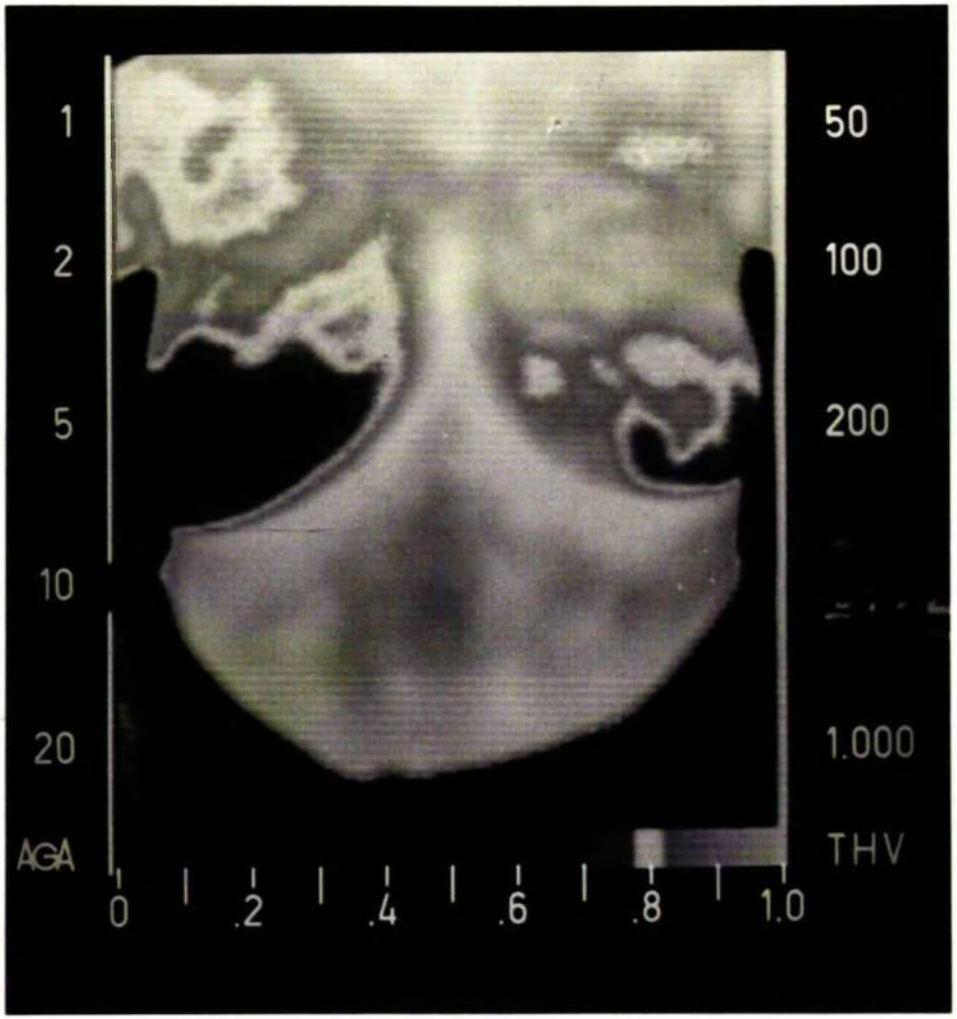
b). Showing isotherms at level 9.



Abnormal thermogram. - generalised increased temperature of left breast. Plates V11a to V11f. show a series of isotherm settings, demonstrating temperature of left breast to be 5 degrees above that of right. Histology cancer.

Plate V11.

c). Isotherms at level 8.



d). Isotherms at level 7.

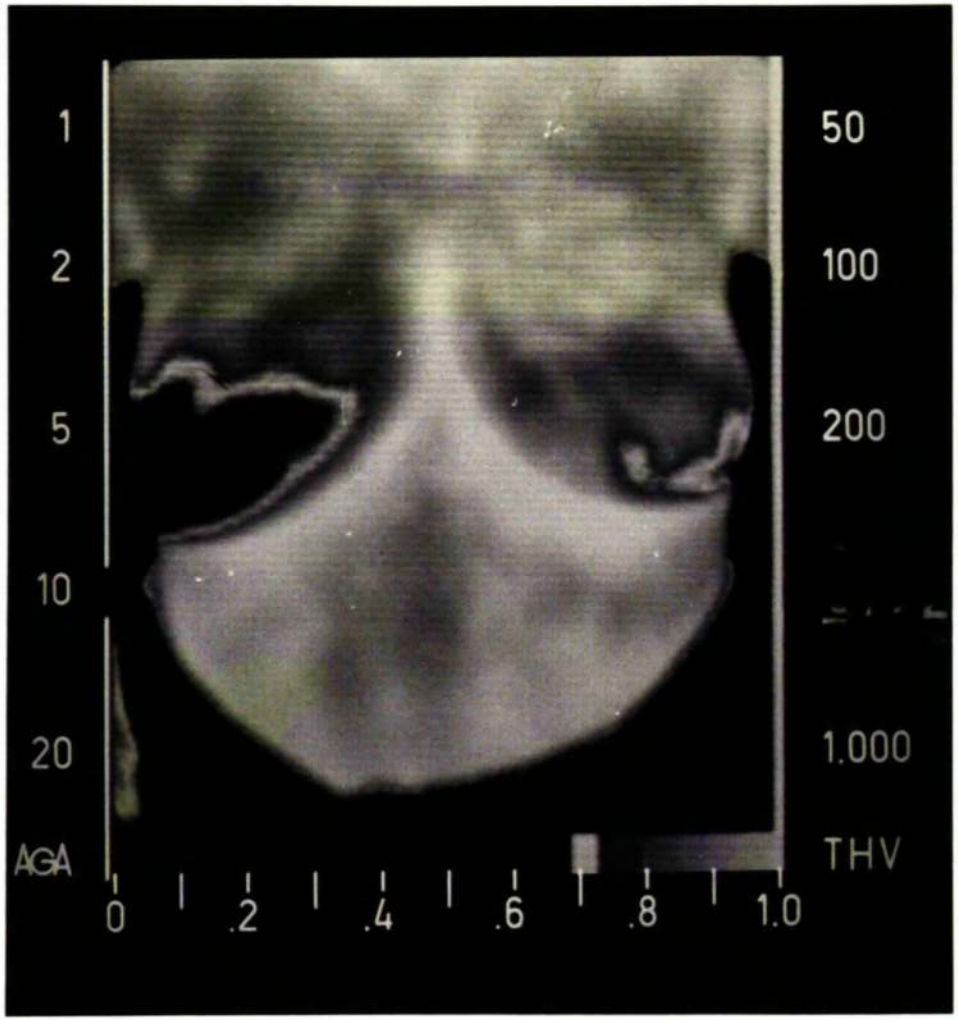
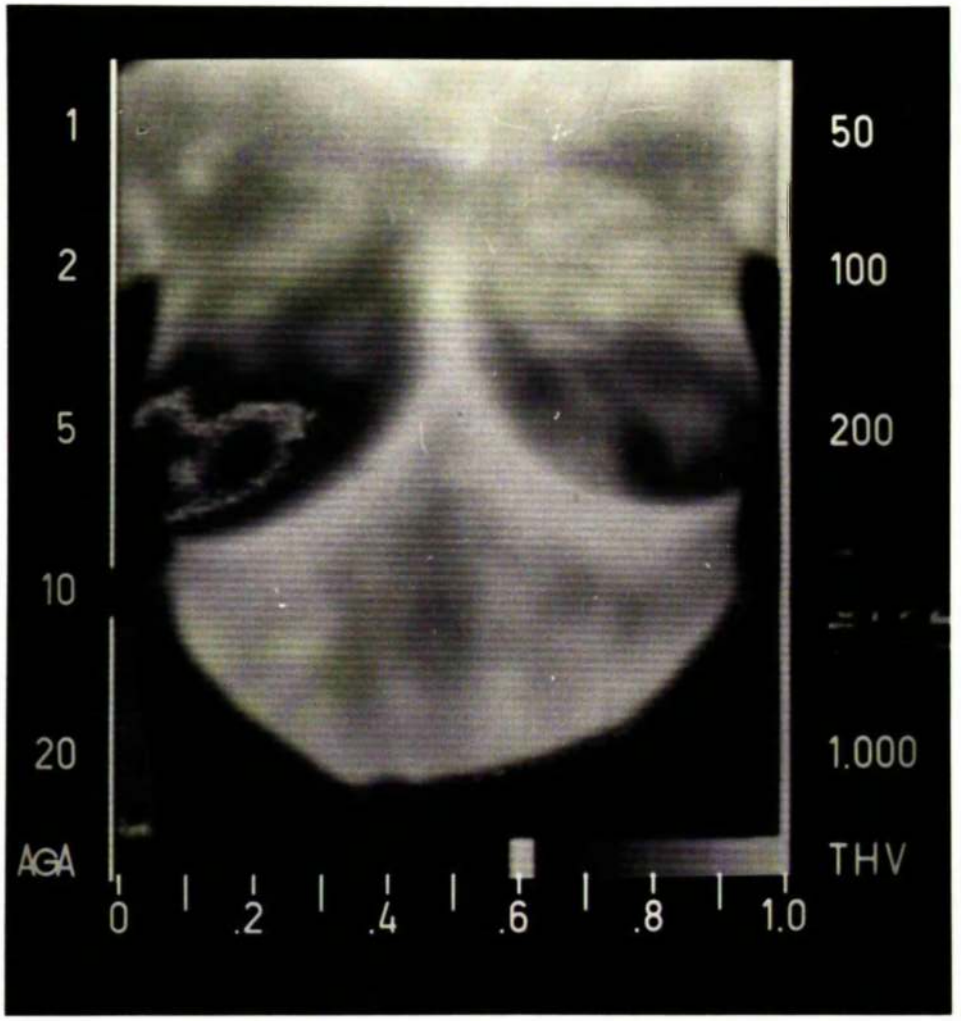


Plate V11.

e). Isotherms at level 6.



f). Isotherms at level 5.

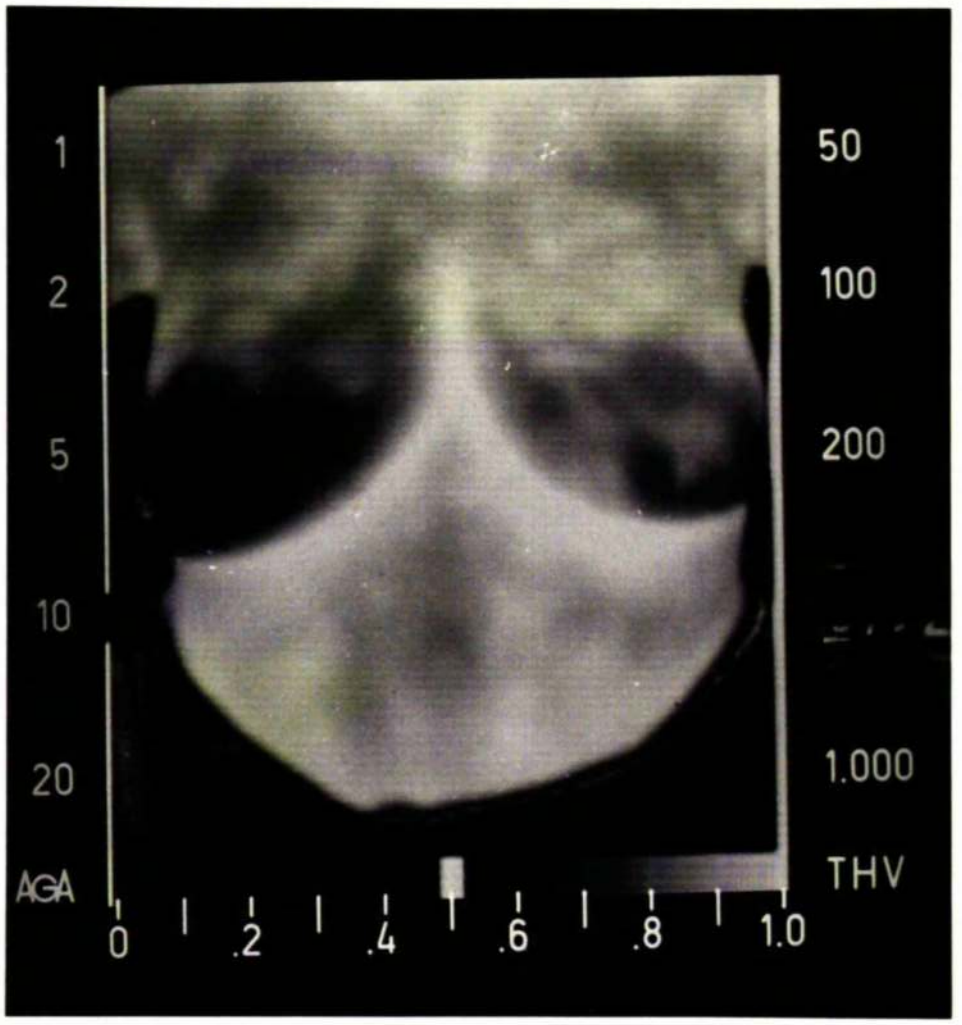
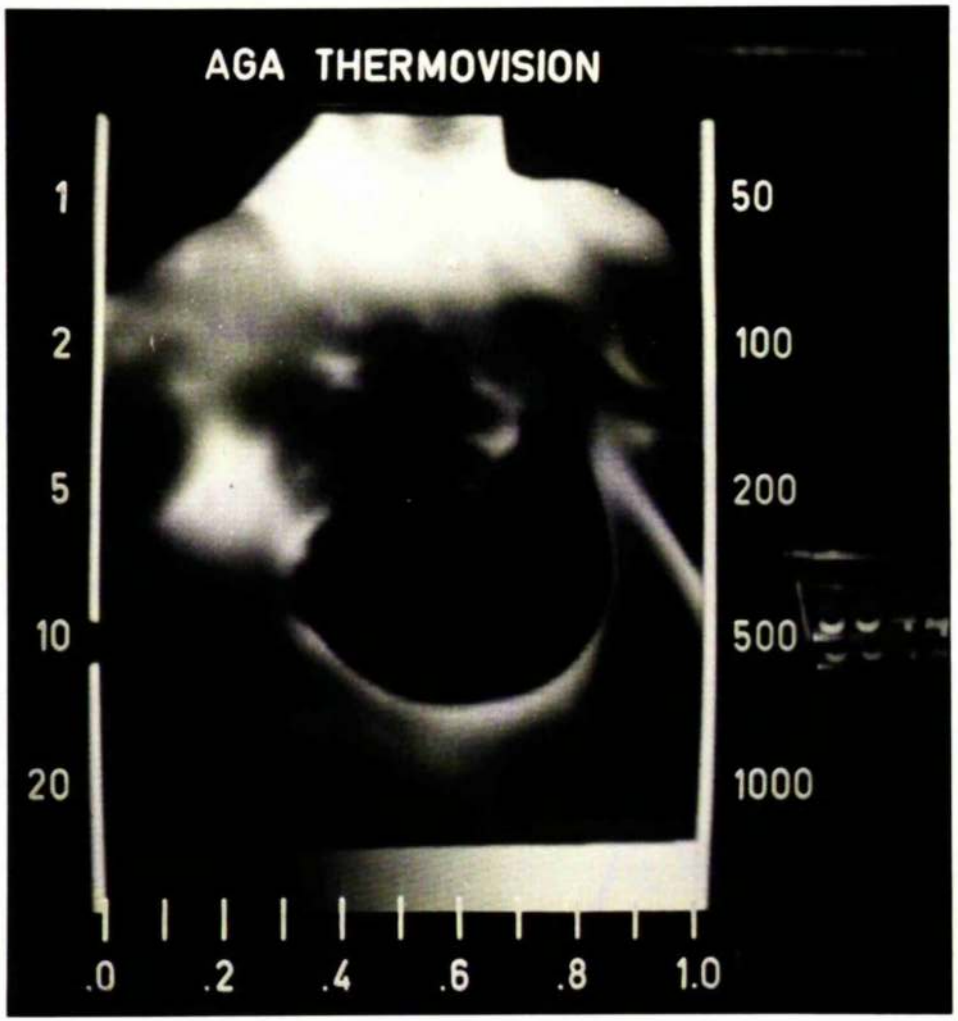


Plate V111.

Right oblique.



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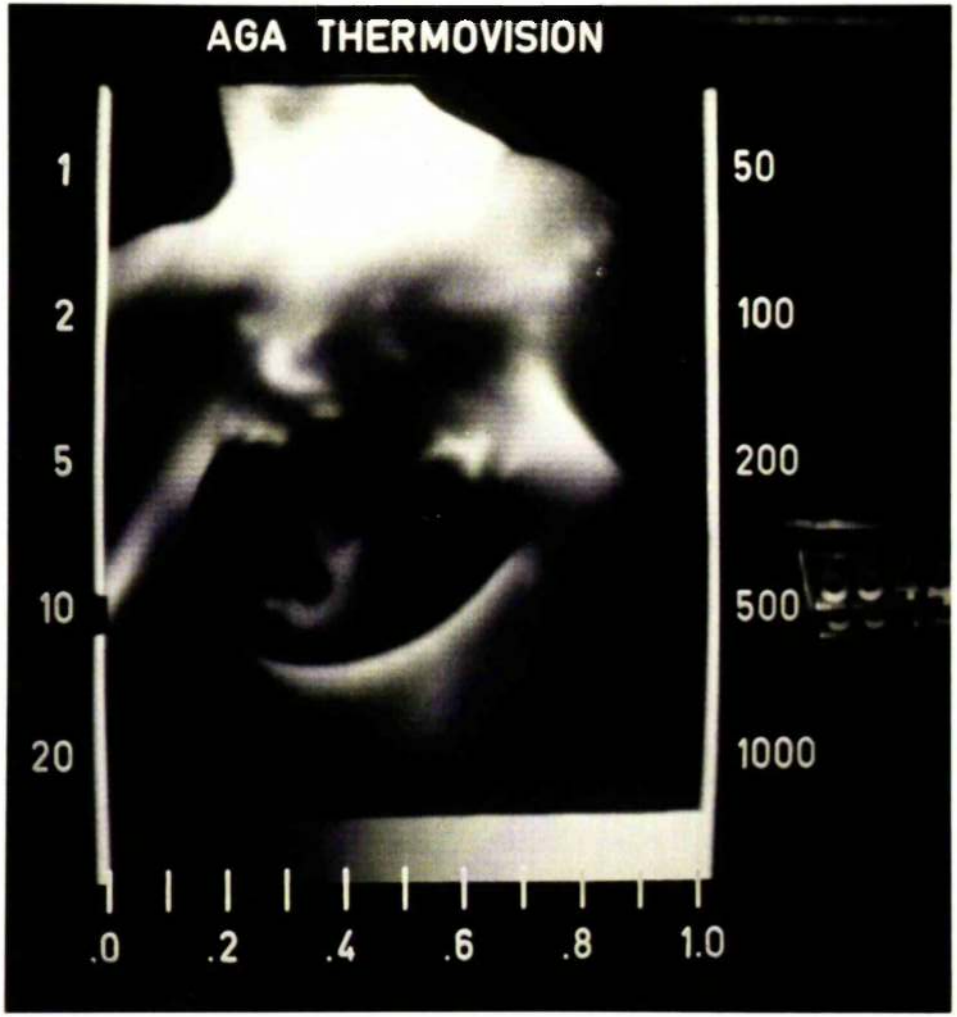
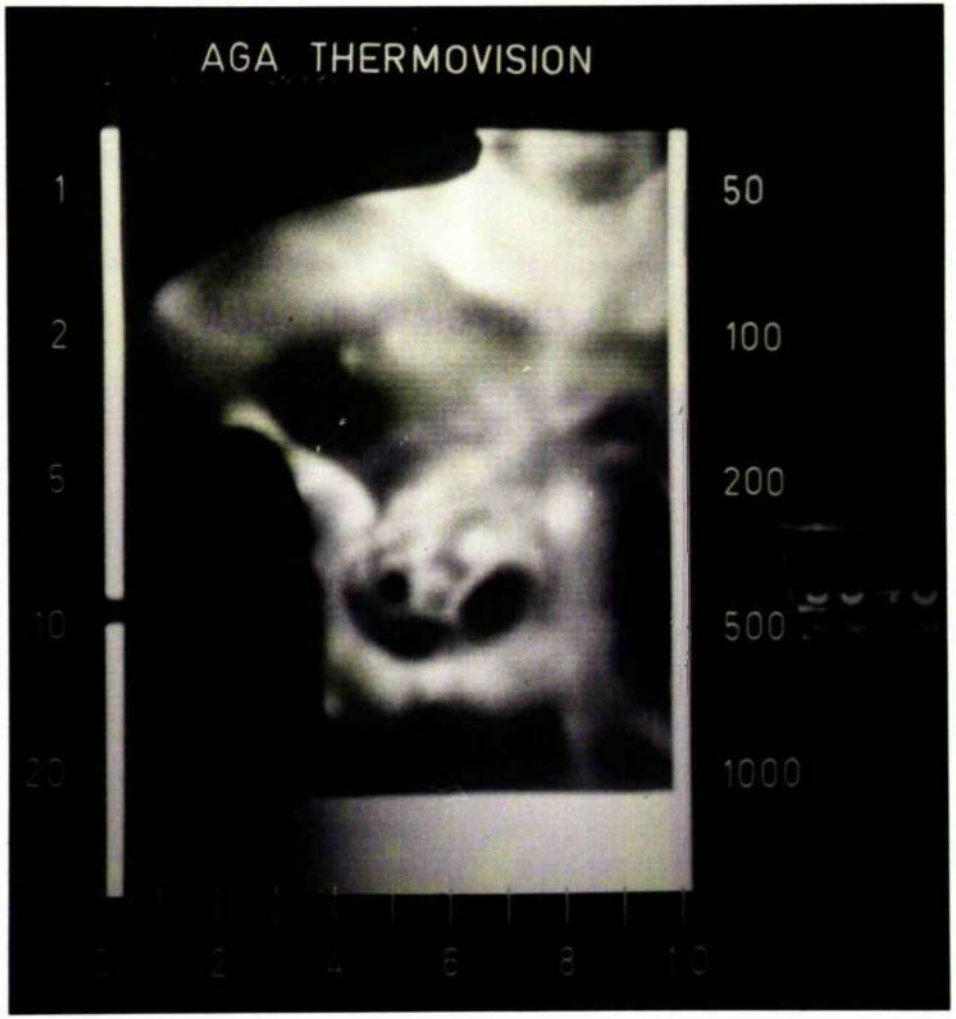


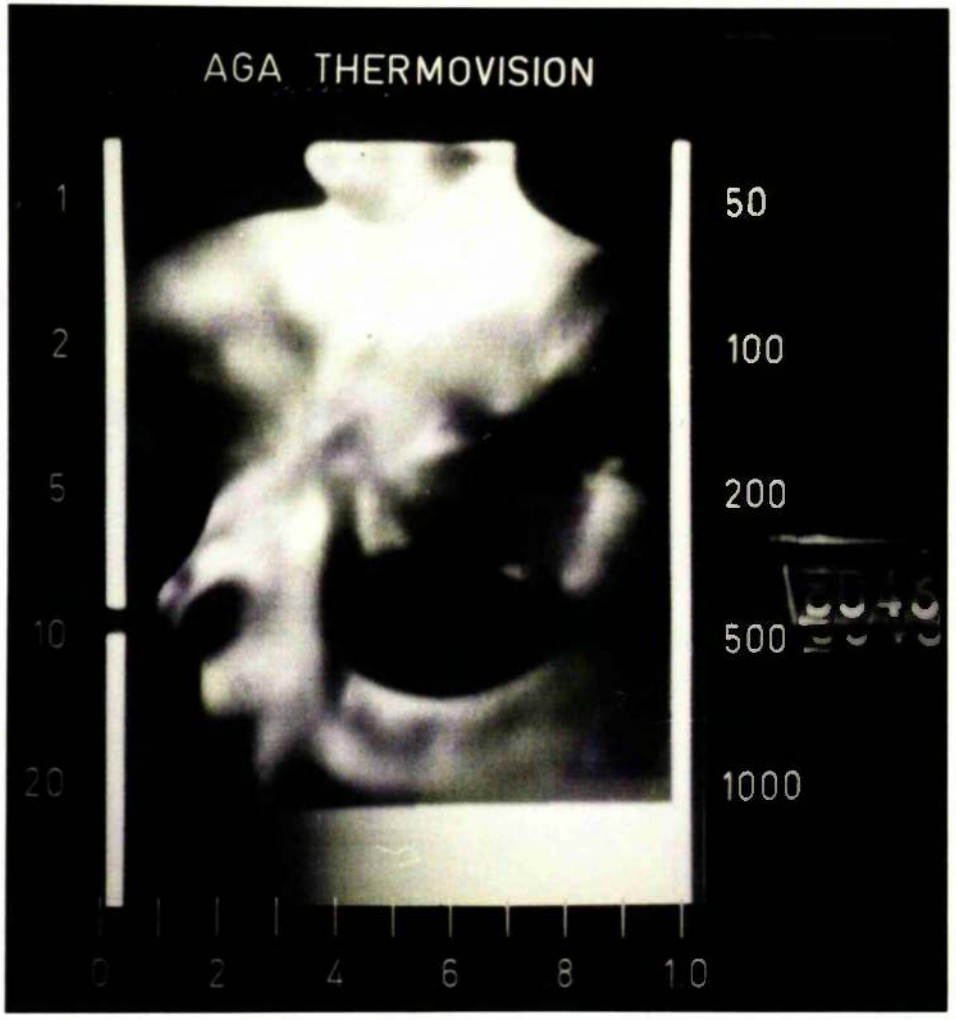
Abnormal thermogram. - hot areola in left breast. Histology cancer.

Plate 1X.

Right Oblique.



Left Oblique.



Abnormal thermogram. - increased vascularity of right breast. Histology - no frank cancer but very active adenosis with many mitotic figures.

A temperature difference of 1.5° or more is significant. Lawson (33) reported a series of cancers where the temperature differential varied from 1.3° to 3.5 with an average of 2.2°. Hoffman (44) considers 1° differential as suspicious and 1.5° and over as positive. In Lloyd Williams' series (45) the majority of the cancers were 1 or 2° hotter.

In general, anatomical surfaces tend to be curved and Watmough et al (46) examined the extent to which the curvature of the emitting surface influences the apparent temperature distribution as measured by thermal scanners. They found that there is an apparent decrease in temperature for surfaces which are viewed very obliquely, at an angle of 45° or more, relative to those areas which are approximately normal to the scanner axis.

This means that on a full anterior view of the breasts, especially if they are tense and large with good curvature, the periphery, viewed obliquely, will be at an apparently lower temperature compared to the central breast.

This is indeed so, but is of no practical value as the definitive point in breast scanning is comparison of contralateral sites - both at

the same angle to the scanner. It does explain, however, why it is difficult to define on the oscilloscope the limits of small flat breasts.

There is no constant relationship between the strength of the signal and the size of the tumour, but it has been suggested that the greater the temperature differential, the poorer the prognosis (38). The greatest differential I have noted was 6° in a large fat breast with a 4 mm. tumour. The temperature differential depends upon the biological activity of the tumour at the time of examination, the depth of the tumour in the breast and the amount of fat.

There may not be a direct spatial relationship between the hot spot and tumour, especially if the neoplasm is deep in the breast and the blood vessels from it do not become superficial over it; a certain amount of the increased heat may pass to the surface along the tissue planes and be directed away from the tumour. Plate V shows a thermogram with a hot spot in the mid outer zone of the left breast. This breast, on senography, showed a cancer high in the upper outer quadrant and this was confirmed histologically.

When a tumour is deep it may give rise purely to a hot areola; the fat layer, a good insulator, is absent at the areola and also there

is a rich anastomosis of the superficial and deep venous systems in the Circle of Haller.

Temperature increases in the breast are not specific to malignancy (44, 45, 47) but occur with any increase in cellular activity, as, for example, in:-

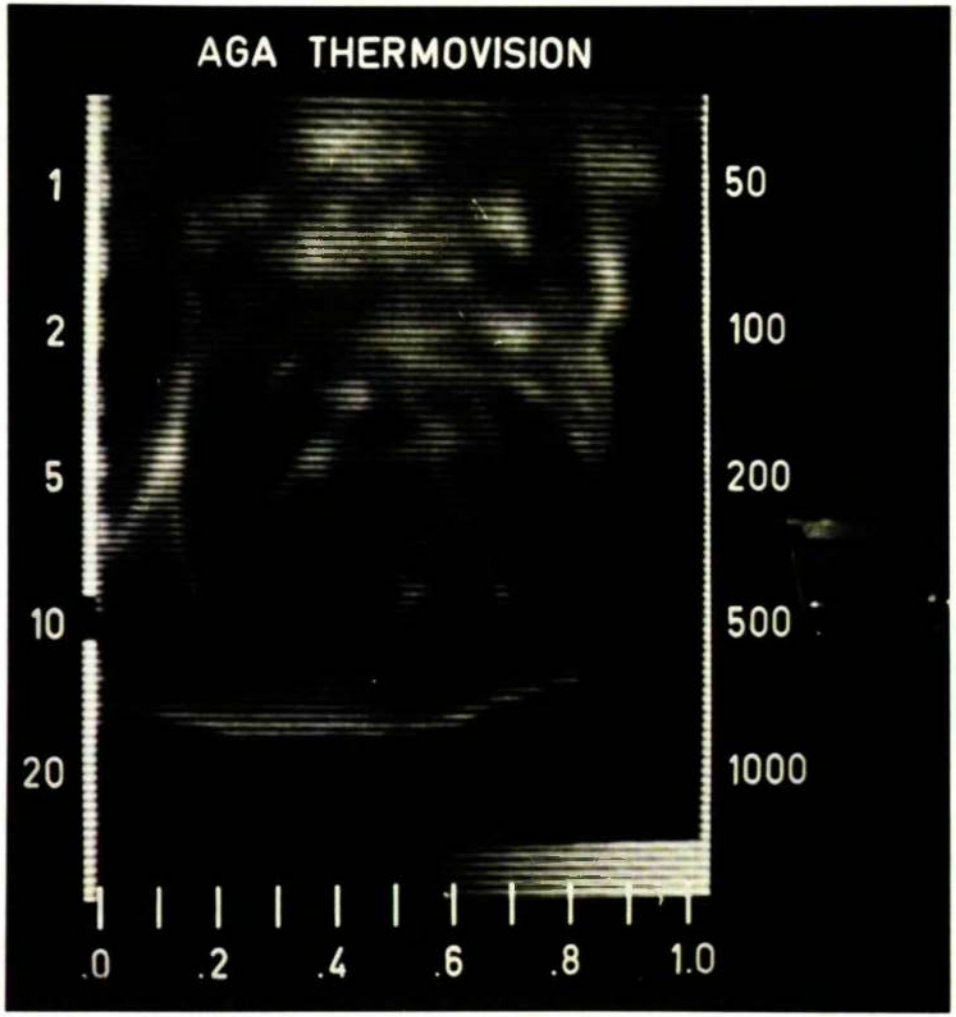
(a) abscesses
(b) some benign tumours, and
(c) some dysplasias

Forrest (7) reported that thirty-seven percent of dysplasias give a raised temperature; according to Draper and Jones (43) 15.5% of dysplasias give a false positive thermogram.

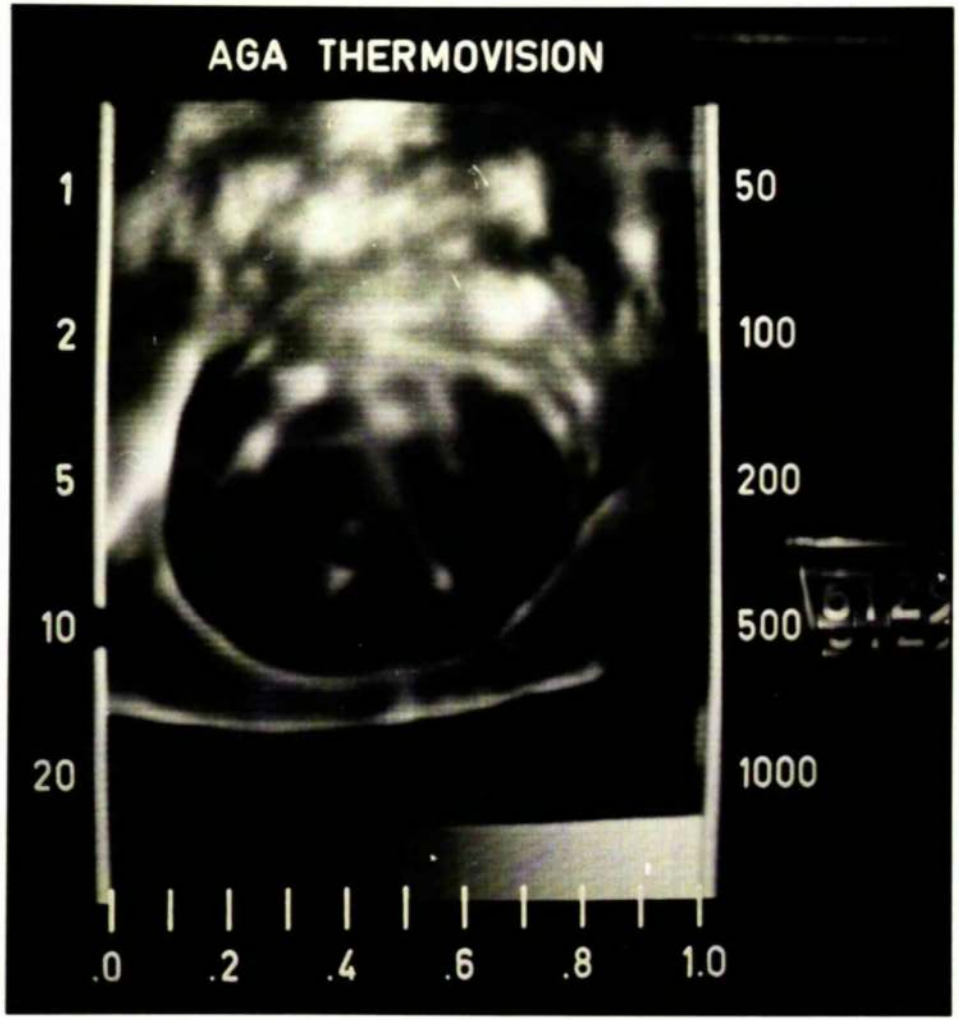
Each individual has a characteristic thermal breast pattern which remains stable over an indefinite time in the absence of changes in hormonal status (Plates X and XI). This fact may well be one of the most useful aspects of breast thermography. When a base line pattern has been established for a woman, any future variation should be considered as a warning. The exception to this is the woman whose basic pattern was established during her reproductive life. After the menopause, a vascular pattern

Plate X.

Left oblique.



Left oblique.



Two thermograms of the same woman, taken at thirteen months interval .

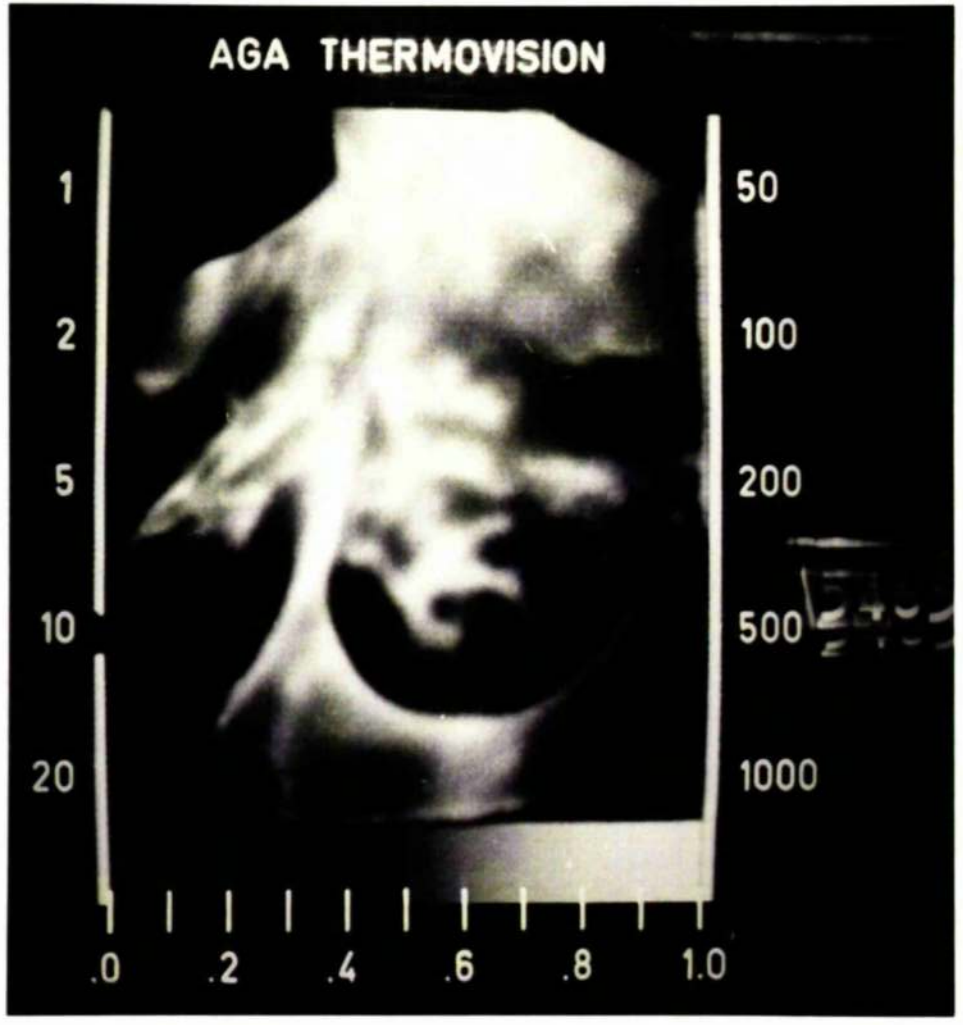
Erratum:-

The preceding thermograms (Plate X) were taken at an interval of twenty-five months and those in Plate XI at thirteem months.

Plate X1.

Left oblique.

Left oblique.



Two thermograms of another woman, taken at an interval of twenty-five months.

may change to a more or less avascular pattern.

Effect of the Menstrual Cycle on Thermograms

Before commencing the survey, this aspect of the work was investigated by taking a series of breast thermograms at weekly intervals; members of the nursing staff acted as volunteers. The basic pattern remained constant but the veins were most prominent just before menstruation and least prominent in the second week of the cycle. In the premenstrual days, some women's breasts have a general increase in temperature which could obscure a hot spot. When this causes difficulty in interpretation of the thermogram, it is worth repeating the thermographic examination between the seventh to tenth day of the next cycle.

Pregnancy causes a very considerable increase in the vascular pattern, to such an extent that interpretation is extremely difficult. For this reason, women known to be pregnant were excluded from the survey. In this respect, there have been two interesting women, to whom I suggested that they might be pregnant. The details are as follows:-

Mrs. N.C.

Aged forty-two. Para 0. Menstrual cycle always irregular, varying from thirty five to sixty days. L.M.P. was thirty five days before date of examination. Her first thermogram, a year

previously, was of the avascular pattern and on this occasion it was highly vascular and symmetrical. Four weeks following the breast examination, she was admitted to hospital with a ruptured ectopic pregnancy.

Mrs. J.B.

Aged thirty-nine. Para 1. Menstrual cycle normal 5/28-30; L.M.P. thirty six days before examination. Again, the thermogram picture was highly vascular and the breasts generally very hot compared to a previous thermogram. She has been delivered of a healthy full time baby.

Effect of Oral Contraceptives on Thermograms

Varying opinions have been expressed on the effect of oral contraceptives on thermograms (and on mammograms). Jones and Draper (43) consider that the pill causes an increased vascularity, so making interpretation more difficult; Hoffman (44) found the pill caused the breasts to be diffusely warm; Harris and Greening (42) and Bilbao (48) state the pill had no effect. I have found great individual variation. The type of pill and the duration it has been taken also appear important.

It was not within the scope of this survey to follow up women purely from the point of view of the effect of oral

contraceptive, and I have been unable to follow individual women at short intervals from first starting the pill.

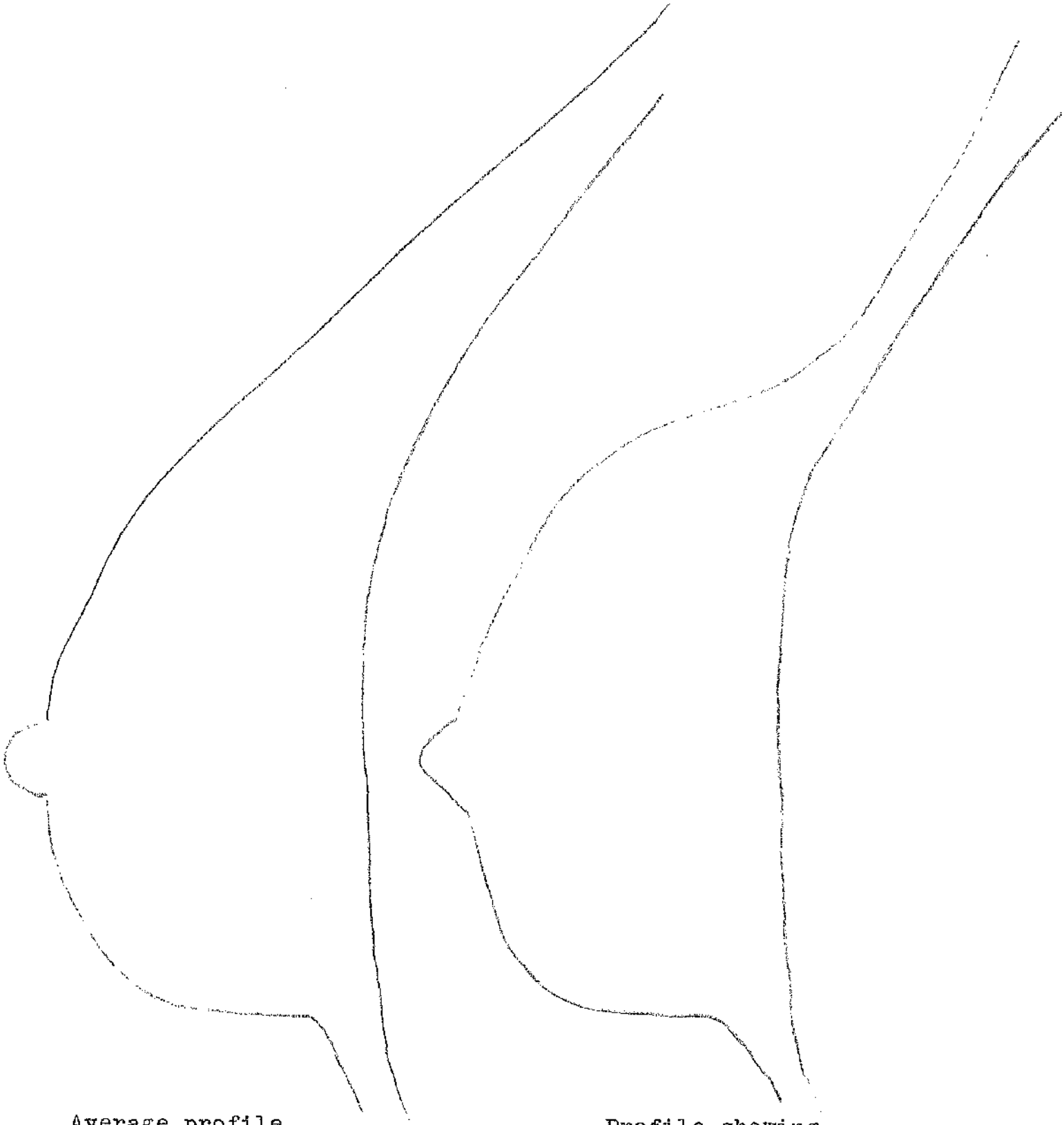
It is my impression, however, that a majority of women have an increased vascularity and warmth during the first few cycles of an oral contraceptive, and thereafter the effect wears off, the pattern reverting to the woman's normal pattern. There appears to be an increased tendency to an avascular pattern when the pill is of a high progesterone type. The following figures support this, although I realise that the numbers are small.

Of 43 women examined within three months of commencing an oral contraceptive, 81% had hot highly vascular thermograms. In a group of 32 women who have taken a highly progestagenic pill (Anovlar or Gynovlar) over a period of 2 to 6 years, 52% had avascular thermograms. (Reference Table No. 5:- The overall frequency of vascular patterns is 65% and of avascular is 25%).

Effect of Breast Contour

Some women with lax, but not necessarily pendulous, breasts, have a sulcus (Figure 4) in the upper outer breast; in this sulcus, which may be considerable in thin women, there may be a pocket of warm air which gives a diffusely warm area on the thermogram (Plate XII). It is bilateral, so should not cause difficulty in interpretation.

FIGURE 4

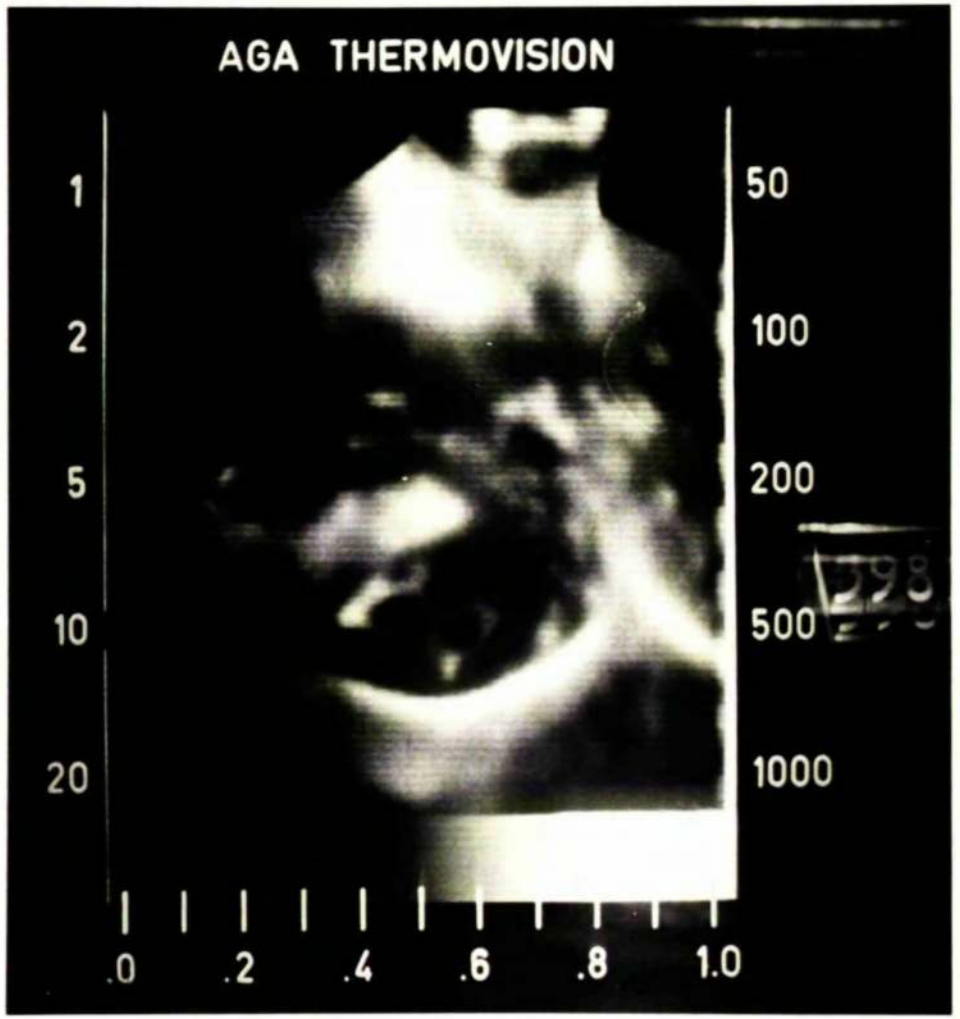


Average profile
from lateral aspect.

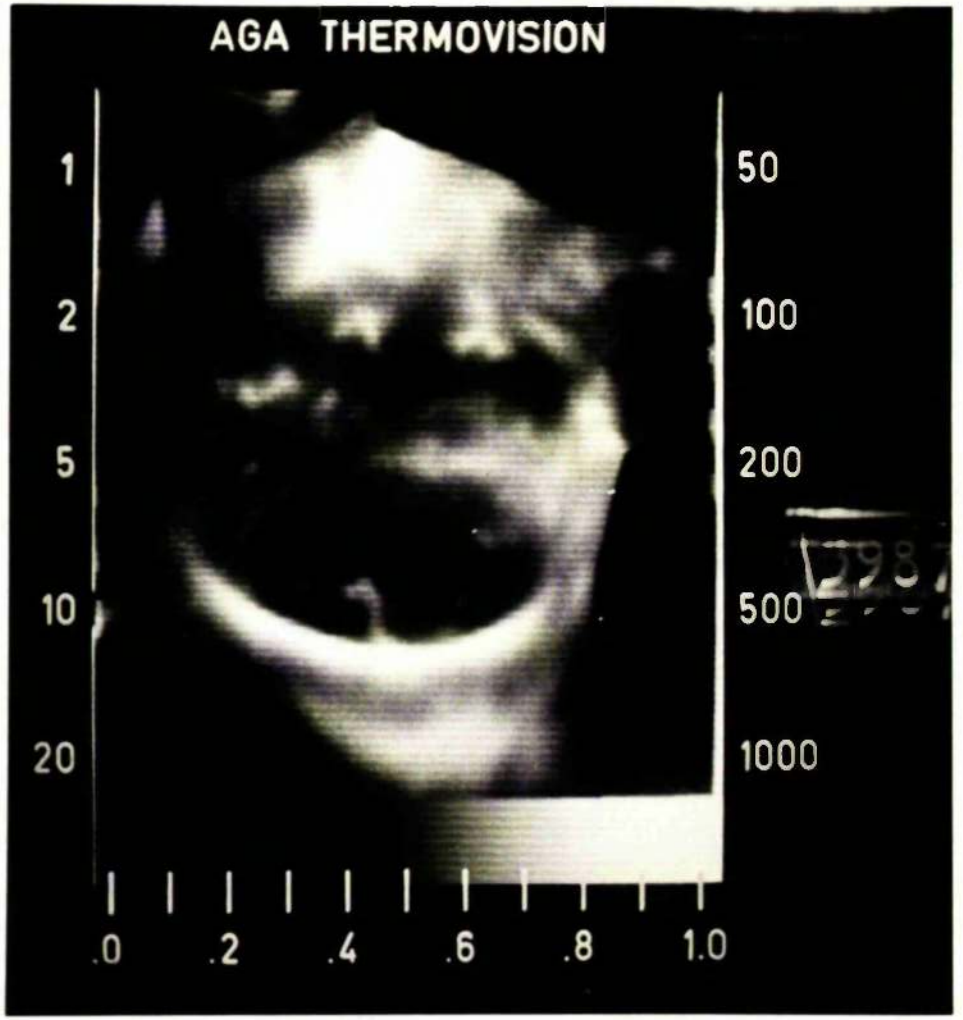
Profile showing
sulcus.

Plate X11.

Right oblique.



Left oblique.



Thermogram showing a warm patch in each upper outer quadrant, in a patient with a "sulcus". She has been reviewed annually over three years and has no clinical findings, a constant thermogram and a negative senogram.

Effect of Nipple Inversion

In an inverted nipple, there again is a pocket of undisturbed warmth which appears as a hot area on the thermogram (Plate XIII). This hot spot could cause confusion especially if the inversion is unilateral and the clinical history and findings are not known. I consider it is essential to make the thermographic diagnosis with the patient present, so allowing for correlation of the history, clinical examination and thermogram.

The nipple is normally the coldest spot on the thermogram, even in cases in whom there is a hot areola. A hot areola is a quite different picture from the hot area due to an inverted nipple.

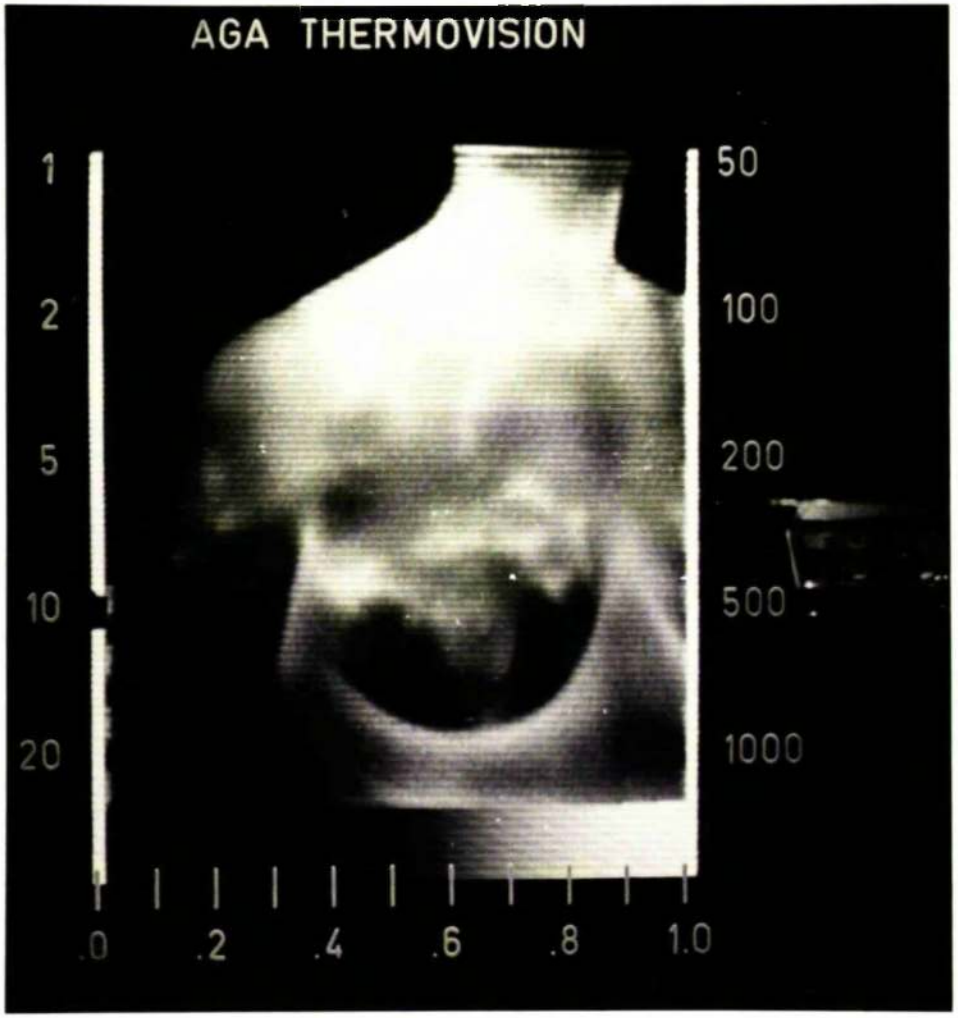
FIGURE 5

Inversion of nipple causing hot spot, nipple not visualised. (ref. Plate XIII)

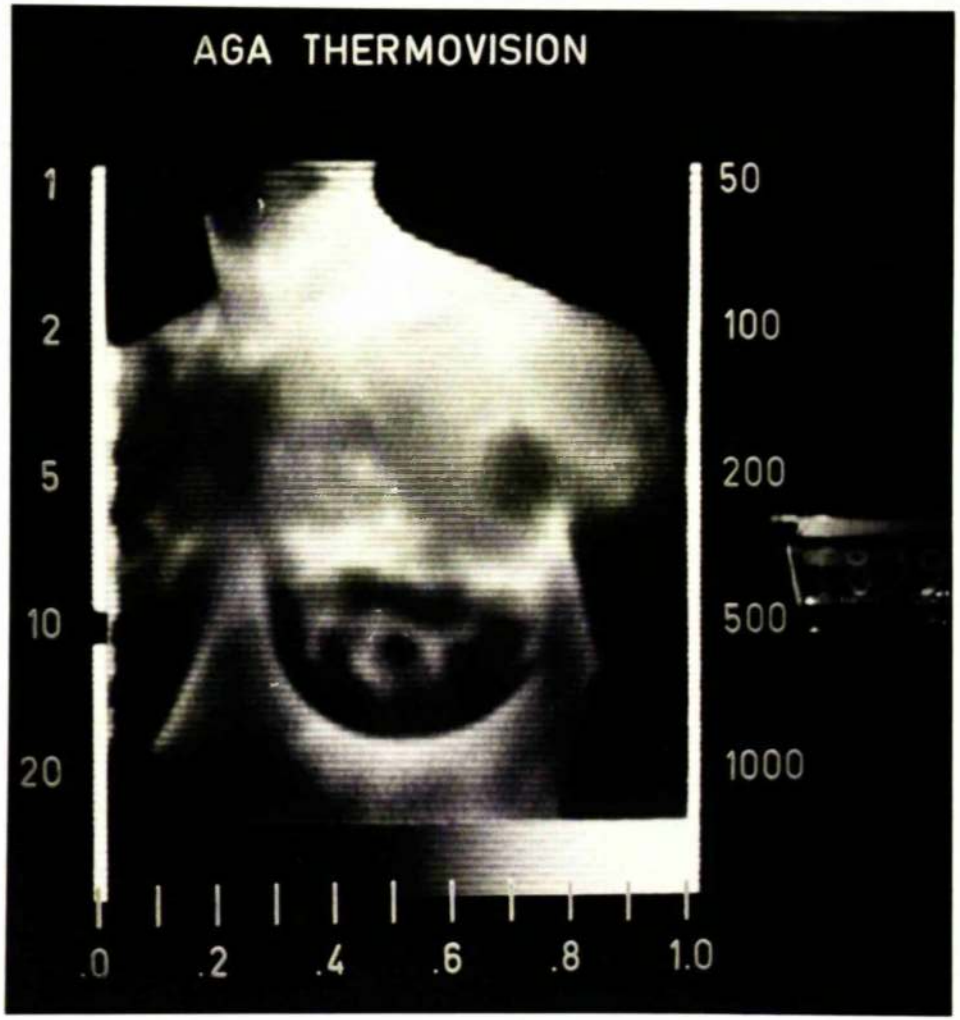
Cold nipple raised temperature of areola. (ref. Plate XIII)

Plate X111.

Right oblique.



Left oblique.



Thermogram demonstrating the difference in picture of an inverted nipple (R) and warmth due to veins of the areola (L).

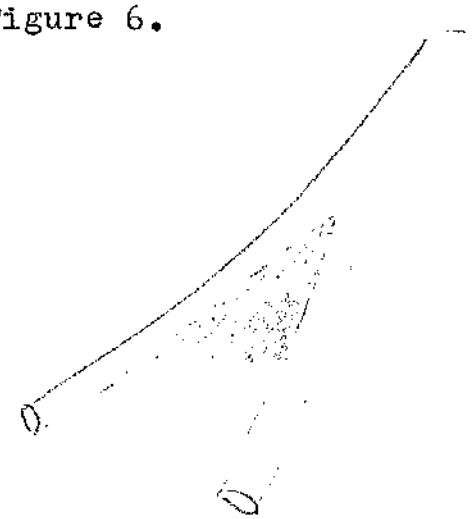
Effect of Asymmetry of Breast Size

In a few women there is considerable difference in the size of the two breasts. When this occurs, the vascular pattern is usually asymmetrical giving an equivocal thermogram, as it must not be assumed that the increased vascularity in the larger breast is only due to the disparity of size.

Effect of Previous Biopsy

As a general rule, a previous biopsy does not result in marked asymmetry of the thermogram pattern, although there may be a reduction in vascular markings in biopsied breasts. When a considerable amount of breast tissue has been removed, however, it may cause asymmetry of breast size and so of vascular pattern. The thermograms of two women with poor scars showed the line of the scar as a cold area.

Figure 6.



Effect of Adjacent Veins

The close proximity of two veins, which are about to unite, may appear to give rise to a hot spot (shaded area) due to the blurring of the heat image with cross radiation. (Fig. 6) By altering the sensitivity of the scan, a crisper picture is obtained and the "hot spot" disappears.

In some Units (49, 50) the thermographic screening is done by a technician who presents a photograph to the medical team for an opinion. I do not agree with this practice and consider that the function of a thermogram photograph is as a permanent record only - to be used for future comparison. The decision should be made at the oscilloscope, scanning at more than one sensitivity, and using the isotherm scale and then correlating the thermographic findings with the clinical findings while the patient is still present, e.g., the question of superficial venous pattern, scars etc.,

(5) MAMMOGRAPHY

Mammography is the technique of examination of the breast using soft tissue radiography, which enables study of minute details of anatomical structure and disease processes in relation to surrounding tissue.

History of Mammography

The earliest breast X-rays were taken by the German pathologist, Salomon (51), who demonstrated details of mastectomy or post-mortem specimens by X-ray, correlating these with clinical findings. No further references appear to have been made to mammography for

approximately twenty years till Warren in 1930 (52) and Seabold in 1931 (53) published results of studying breasts by soft tissue X-ray. In 1938, Gershon-Cohen (54) published his early work on this subject. It was Leborgne's monograph (55) in 1953 which established the validity of mammography. During the last seventeen years, there have been many papers on the subject in America by Gershon-Cohen and his colleagues - Hordes (56), Ingleby (57, 58), Berger (59) and by Egan (60) and in Europe by Gros (61), Samuel and Young (62), Samuel (63) and Young (64).

The technique of mammography has been accepted slowly because

(1) until relatively recently equipment has been inadequate to produce the films of the high quality required for accurate diagnosis;

(2) to produce good films and interpret them has been very time consuming, and

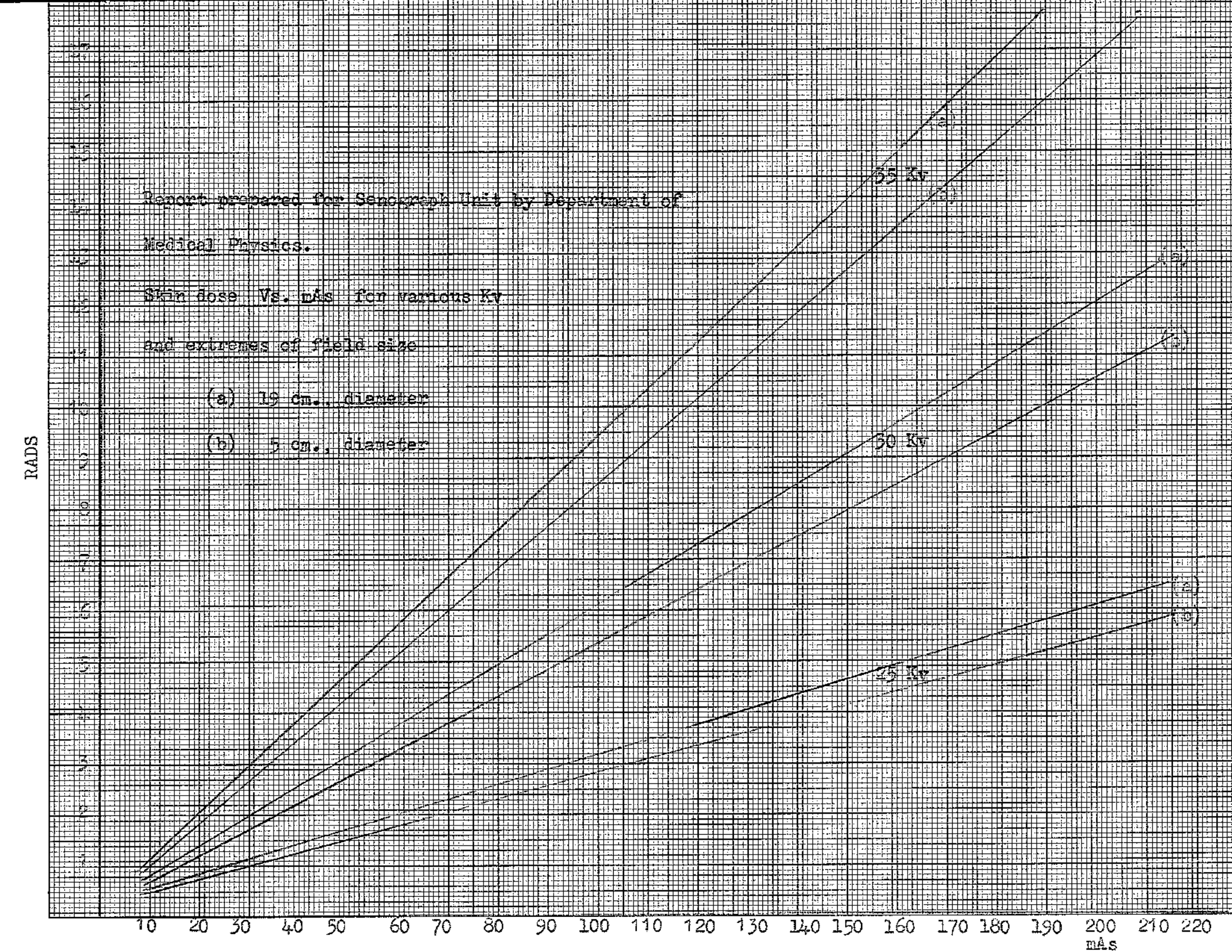
(3) surgeons have not shown much interest, not appreciating the potential of mammography; even today, many surgeons are not interested in the pre-clinical cancer which they cannot feel.

For the first two years of this survey, the mammography was done at the Royal Victoria Infirmary, Newcastle upon Tyne, by

Dr. P. Hacking. Conventional equipment, modified to give a reduced KV of 25-35 was used with Ilford Industrial B and Ilfrex film. Two views, supra-inferior and lateral were taken of each breast; markers 'R' and 'L' were placed in each upper outer quadrant for ease of identification.

In December, 1969, a Senograph was installed in the Well Women Breast Unit. This equipment was designed by Professor Gros of Strasbourg, especially for mammography. It is a low voltage, constant potential X-ray with a molybdenum target which gives films of good contrast and sharpness because of a monochromatic ray of optimum wavelength for soft tissue X-ray. All the useful output of the senograph is in the correct range and no unnecessary radiation is given to the patient (65).

X-ray pictures of excellent quality can be quickly and easily obtained with the Senograph and Kodak Crystallex Film - a film of fine grain. Before deciding to use Kodak Crystallex film for this survey, several trials were done with a selection of different films and using various exposure factors and processing techniques. For this work a breast Phantom was used.


Report prepared for Senographh Unit by Department of
Medical Physics.
Skin dose Vs. mAs for various Kv
and extremes of field size
(a) 18 cm., diameter
(b) 5 cm., diameter
RADS
55 Kv
50 Kv
45 Kv
(a)
(b)
10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220
mAs

The films are hand processed with care to avoid all risk of artifacts etc., so maintaining the high quality of the film. They are developed for four minutes at 68°F. An acid stop bath is used to stop development and prevent streaking, the films being agitated in the bath for approximately thirty seconds. Fixing must be permitted for a minimum of fifteen minutes before being washed in running water for a further ten minutes.

The Senograph is easily handled and is convenient for the patient in that the tube can be made to rotate through 360° and the patient remains seated on a stool which is adjusted for height. It is a feature of the Senograph that moderate compression of the breast is used, between the base plate with the film and the cone. The tube is water cooled and continuous use over two to three hours is possible.

X-ray Dose

After installation of the Senograph, Professor Farmer, the Department of Medical Physics, University of Newcastle upon Tyne, was asked to assess the dosage and possible scatter. Tests confirmed Gros' (65) specification (see copy of graph) as to dosage and the fact that there is virtually no scatter. The average factors used in the survey are 25 to 30 KV, 25 to 30 ma., and 1½ to 2 seconds.

Five cones are supplied with the Senograph; they vary in diameter from 5 to 19 cms. This gives an average skin dose per exposure of 2.5 to 3r.

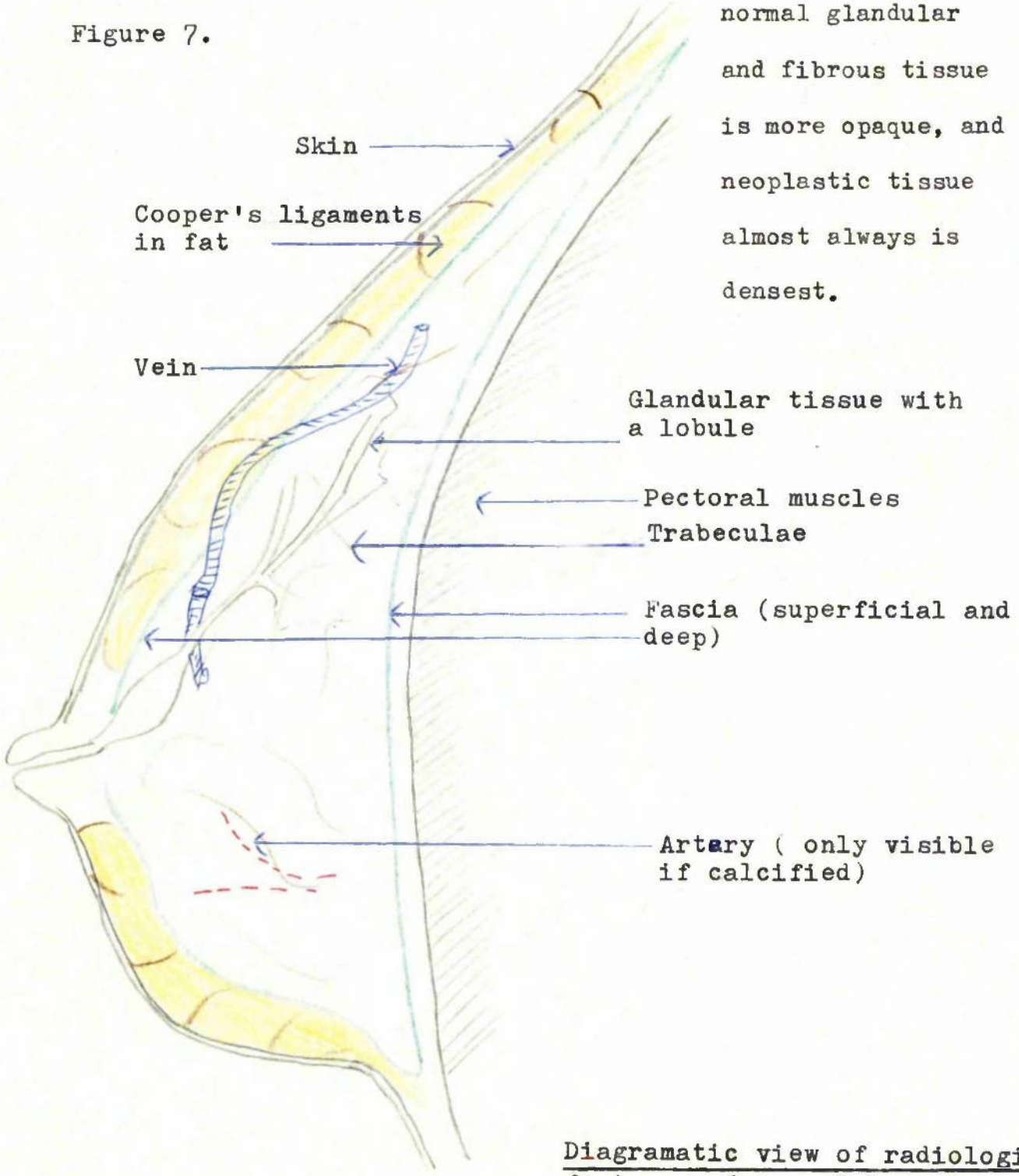
The density of the breast is more important than size when deciding the factors to be used, the dense glandular breast requiring more penetration than the large fat breast. Compression of the breast gives better definition and prevents movement. The mammogram films are screened on a high intensity viewer with variable illumination; moderate illumination is used to assess the general features of the breast and possible opacities. Microcalcification is excluded, using a hand lens and high illumination.

The Normal Breast

The breast is composed of a lobulated mass of glandular tissue, traversed and supported by strands of fibrous tissue. The glandular tissue comprises fifteen to twenty lobes, radiating from the nipple. Apart from the areola and nipple area, the breast is covered by a layer of fat; there is also a variable amount of fat in the interval between the glandular lobes (Cunningham's Anatomy) (66). The relative and total amounts of glandular tissue, fibrous tissue and fat vary according to hormonal influences.

The ratio of fat to glandular and fibrous tissue is most important from the radiological point of view. Fat is radiolucent, normal glandular and fibrous tissue is more opaque, and neoplastic tissue almost always is densest.

Figure 7.



Diagramatic view of radiological features of normal breast.

Radiological Appearances of Normal Breasts

There are four types - immature, glandular, involutional and atrophic.

The immature breast, as seen in adolescence, and which sometimes persists into the early twenties, is homogeneously dense with a smooth surrounding border of fat. Trabeculae may be faintly visible.

The mature glandular breast, as seen during the reproductive period, is less dense, there being a variable amount of fat interspersed with the glandular tissue. The lobules occupy, in the main, the base and periphery of the breast; the principal density is found at the base, is broad and rather fluffy in anterior outline. The sub-areolar area contains the lactiferous ducts only, as cord-like structures.

The trabeculae run from the base of the breast towards the nipple and in some women Cooper's ligaments are also readily seen.

The involution type of breast occurs with the hormonal changes of the menopause. There is gradual involution of the lobular tissue and a relative increase in the fibrous trabeculae and fat. The remaining glandular tissue, usually in the upper outer quadrants, appears as patchy opacities.

The Atrophic Breast

In post-menopausal women, there is usually further replacement of glandular tissue by fat and the trabeculae become progressively thinner.

The veins of the breast are clearly outlined on X-ray, because of surrounding fat; the arteries, without this enveloping fat, are only visible when they become calcified. The skin is depicted on the mammograms and skin changes are discernible.

X-ray Signs of Malignancy

A. Primary Signs of Carcinoma

(1) An opacity of increased density, greatest at the centre, due to replacement of breast tissue and fat by denser cancer cells and reactive fibrosis. A mucin secreting cancer is the least dense and then the diagnosis may depend on secondary signs.

(2) Shape of Opacity

(a) spiculated or stellate due to

(i) retraction of trabeculae towards the lesion - caused by cancer cells exciting irregular fibrosis, i.e., scirrhous in type

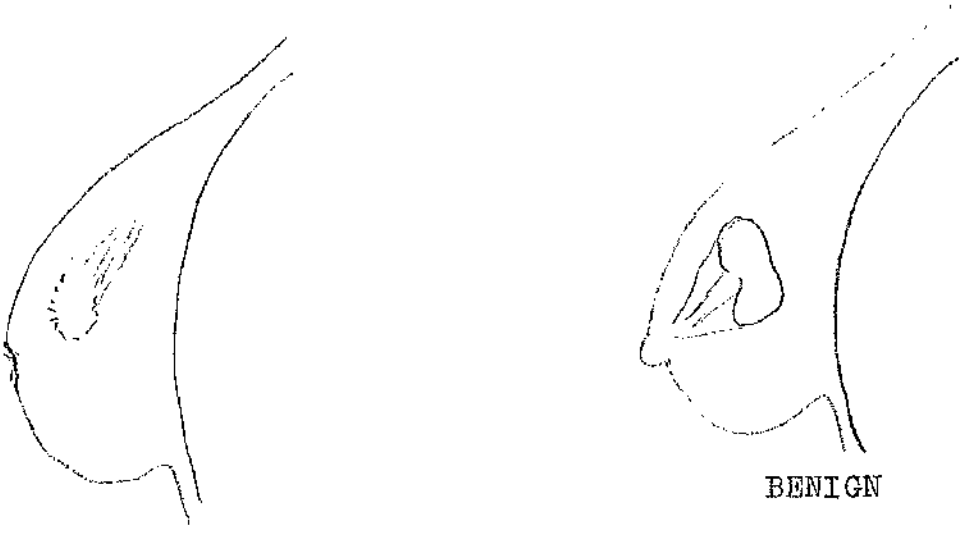
(ii) strands of cancer cells in ducts and/or lymphatics

(iii) thickened peri-ductal connective tissue

(b) For a time, the opacity may be well circumscribed but when viewed in more than one projection, it is usually indistinct or irregular at some point. The circumscribed cancers are the mucin secreting, the medullary, or the intra-cystic cancers.

(c) There may be a comet tail to the opacity, the tail flaring out from the opacity and due to invasion and retraction. It differs from the convergence of trabeculae seen anteriorly to a benign lesion.

FIGURE 8



MALIGANT BENIGN

(d) A malignant opacity may have a clear halo due to surrounding oedema. This is different from the clear edge of radiolucent fat, pushed aside by an expanding benign lesion, which is frequently densest at the periphery.

(3) Size of Opacity

Egan states (67) that a highly invasive cancer rarely exceeds 3 cm on X-ray. Beyond this, the changes of reactive fibrosis, oedema and skin thickening are so diffuse that it is not possible to measure the primary lesion.

A palpable mass obeys Leborgne's Law (55) which states that a malignant tumour feels much larger clinically than it appears on X-ray, whereas a benign lesion feels and appears of equal size, clinically and on X-ray. The explanation of this is that X-ray outlines the tumour only; the mass felt clinically includes the tumour and, if malignant, the surrounding breast tissue being invaded by it with reactive oedema and fibrosis.

(4) Calcification

As an indication of malignancy, calcification should be bizarre, varying in shape, size and density, punctate, uncountable and localised. It may be associated with an opacity but in the case of an early intraduct cancer, calcification may be the only indication of malignant change and can be demonstrated in lesions as small as 5-10 mm.

Other causes of calcification are:-

(1) epithelial hyperplasia. According to Egan (67) one-third of those mammograms with fine stippled calcification are due to this, and only histology can exclude malignancy. In many cases the hyperplasia is associated with a minute carcinoma, if enough sections are examined histologically.

(2) Amorphous calcification occurs in degenerating fibroadenomata; it is coarse and quite unlike the calcification of malignant type.

(3) Coarse intraductal calcification which appears as isolated and widely scattered rings or streaks, occurs in conditions, e.g., some dysplasias or trauma, which are associated with fatty degeneration. This causes the formation of calcium soaps with the deposition of calcium phosphates and carbonates (68).

(4) Mulberry-like calcification in a large duct indicates an intraduct papilloma.

(5) Egg shell type of calcification may occur in a cyst wall. (4) and (5) are rare according to Egan (67). I have seen each on one occasion only in over 3000 women whose senograms I have examined.

(6) Trauma or biopsy may produce tiny calcification in subcutaneous tissue and is extra glandular.

(7) Old inflammatory conditions may be the cause of coarse calcification in necrotic or fibrous tissue.

(8) Arteriosclerotic vessels may show calcification.

To demonstrate malignant calcification, films of excellent quality are essential. Coarse grain film emulsion must be avoided as the grain size may be as large as small calcifications. For accurate diagnosis, films must be viewed with a magnifying glass, as significant calcification may be as small as 0.05 mm. (This does not reproduce well in photographs).

Calcification is the most important single radiographic sign in the diagnosis of pre-clinical breast cancer. The incidence of

calcification associated with breast cancer has been reported as occurring in 42% of specimens of breast tissue examined by Black and Young (69), 70-90% by Egan (67), 75% by Shepard (70). Young and Samuel (62) were able to demonstrate calcification in only 39% of breast tumours examined by mammography, and comment that it is less easy to demonstrate calcification in vivo. Egan drew attention to this also, his in vivo figure being 35%-45% (67).

With improved equipment, i.e., the Senograph, it was hoped that it would be easier to demonstrate calcification in vivo, as Gros' figure of 70% suggested (61). This has been proved correct as my results will show.

Why calcification should occur in such a high proportion of breast cancers is uncertain. Samuel (63) suggests that it may be related to the presence of calcium in the normal secretion of the breast. Egan (67) suggests that actively growing breast tumour cells may have a higher affinity for minerals than normal cells, so increasing their calcium content.

B. Secondary Signs of Cancer

(1) Increased Vascularity

On X-ray, increase in diameter rather than number of veins is important and Egan (67) found this a valuable sign in fifty

percent of cancers. Increased vascularity may also occur in benign conditions, e.g., an infected cyst and sometimes in dysplasias but is usually of lesser degree. Wallace and Dodd (71) propounded their theory of the Venous Diameter Ratio, i.e., diameter vein in affected breast: diameter vein in normal breast. They found that in seventy seven percent of eighty eight cancers this ratio was 1.4 to 1 or greater, and less than 1.4 to 1 in 87.6% of ninety seven benign lesions.

I have not found the Venous Diameter Ratio of practical value. To make the measurement of vein diameter, I have used a linen counter with a magnified transparent scale. The probable reasons for its inaccuracy are:-

(a) the same vein can vary in diameter within a short distance

(b) the vein to be compared on the contralateral site ought to be in the same plane. It is not possible to ensure this - anatomically or radiographically.

Nevertheless, there is no doubt that an overall impression of increased diameter of the veins in an area is a very helpful sign and can draw attention to a very small lesion.

(2) <u>Oedema or thickening</u> of the skin associated with malignancy may be noted on X-ray before being clinically apparent. This

may occur over the tumour, or in deep seated cancers it may first appear just inferior to the areola in the dependant area of the breast.

The skin thickening sometimes found on mammography in the area of the infra mammary fold of large pendulous breasts, is due to compression and is bilateral. In old women, atrophy of the skin may cause variation in skin thickness on X-ray. Skin thickening may be due to a previous biopsy and the site of the latter must be known to exclude this cause.

(3) Wolfe (72) suggested that a localised prominence of duct pattern is an important indicator of an early lesion. The ducts in the vicinity of a mass or between an opacity and the nipple are frequently prominent due not to dilatation, although they may be full of cancer cells, but to deposition of collagen round the ducts. Jackson and Orr (73) consider that collagenosis is of great significance as a pre-malignant sign, especially if it is accompanied by epithelial hyperplasia. They suggest that the collagenosis is a reaction to a neoplastic stimulus and a defence response. Again, this is a helpful sign in drawing attention to a very small lesion especially in a rather dense breast.

(4) Changes in breast architecture:-

(1) Loss of subcutaneous fat stripe

(2) distortion of normal curve of Cooper's Ligaments, which traverse the fat stripe. This can be a most helpful pointer in a dense breast which may obscure a lesion

(3) skin and nipple retraction

(4) straightening of ducts

(5) overall increase in density

As with thermography, the essential for diagnosing the smallest lesion is comparison with the other breast or with previous films.

MATERIAL AND ORGANISATION OF SURVEY

The survey falls into three phases:-

Phase 1 — Clinical examination, with mammography in selected cases.

Phase 11 — Clinical examination and thermography, with mammography in selected cases.

Phase 111 — Clinical examination, thermography and mammography, in a highly selected group.

Phase 1

While arrangements were being made to open the Well Women Clinic for the Detection of Early Breast Cancer, it was decided to

offer breast palpation to those women aged forty years and older, attending one of the Well Women Clinics for cervical smears run by the Women's Cancer Detection Society. Seven hundred women accepted this offer.

Phase II

The work of the Women's Cancer Detection Society in the field of cervical cytology was well known in the North East of England and it rapidly became known, by word of mouth, that a "Well Woman Breast Clinic" had been opened. In contrast to the experience of Minkler (74), who found women unwilling to come forward, a waiting list for appointments built up rapidly. In view of this, the appointment secretary was instructed to emphasise to women requesting a clinic appointment that the survey was for well women, that if they had any symptoms, their family doctor should be consulted, and that they should not delay until seen at the clinic.

In the first nine months, the only limitations were that the woman should be symptomless, not pregnant, and live within a radius of a hundred miles from the Unit. Later, women under thirty-five years were excluded. Only 1.8% of breast cancers occur in women under thirty years of age (75), and 3% in those under thirty-five (76). This was one way of reducing the numbers demanding appointments.

The exception to this ruling is the woman with a family history of breast cancer. Epidemiologists (76, 77, 78) agree that this is a familial disease, and Papandriamos (79) showed that the daughters and nieces of victims developed breast cancer on average ten to twelve years earlier than the older generation, although the work of Smithers (80) does not confirm this.

All women were seen by appointment. Twenty-five women could be examined each session, and appointments were made at ten minute intervals.

On arrival, the woman was met by the receptionist, who completed the non medical details of the history sheet and conducted the woman to her cubicle. She instructed the woman to strip to the waist and sit with the arms resting on the chair arms. As well as this verbal instruction, each woman was given a printed form repeating the instructions, and explaining the need for the cooling period. On the wall of each cubicle is a picture showing how to sit while cooling (Plate 1). After the pre-scan cooling period the woman was given a disposable paper cape, and, walking with arms akimbo, was escorted to the thermography room. Each cubicle has a numbered key so that only the key required to be carried by the individual, in the knowledge that her belongings were secure.

Position for Thermography

This was done with the woman standing arms akimbo. Each breast was scanned in the lateral oblique view including the axillary tail, and then an anterior view of both breasts was done.

With the original Aga Thermovision, it was necessary to refocus the machine between the lateral oblique views and the anterior view. Since acquiring the latest model (680) which has a shorter focal length and wider angled lens, this is no longer necessary and simplifies proceedings considerably.

I have always felt that the large pendulous breast never cooled adequately, remaining warm in the infra-mammary fold. In an attempt to overcome this, varying positions were tried - without practical success. I tried scanning with the woman lying on a couch with a pillow under the scapula to scan the ipse-lateral breast, in the hope that spreading the breast over the chest wall would help. This did not work nor did raising the foot of the couch as the really pendulous breast just falls into the axilla. (Figure 10). The only position in which the infra-mammary area would cool was the knee elbow position and this was not acceptable to the women.

FIGURE 9

Position for thermography Patient standing

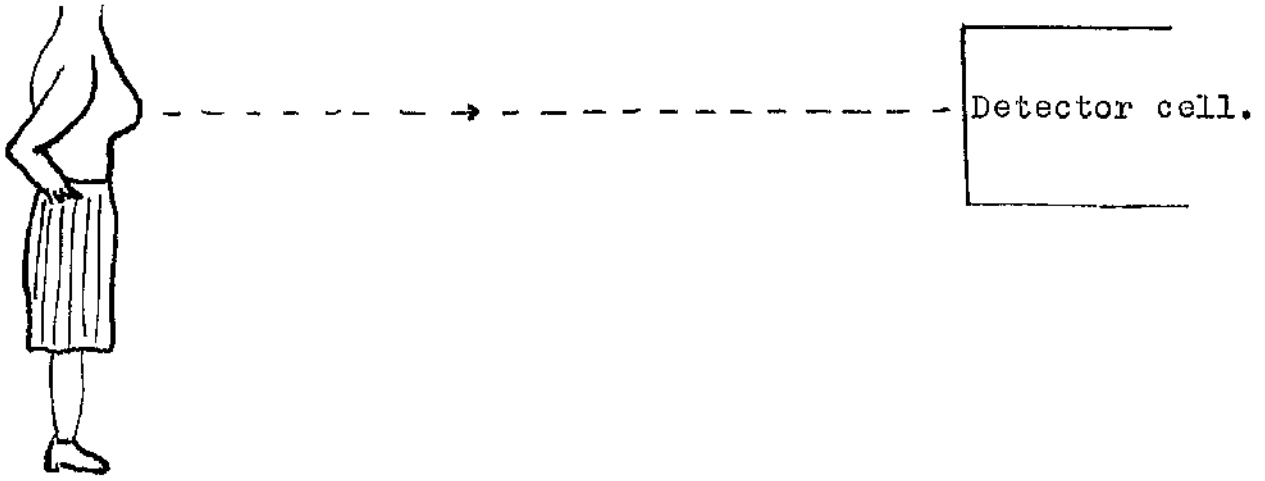
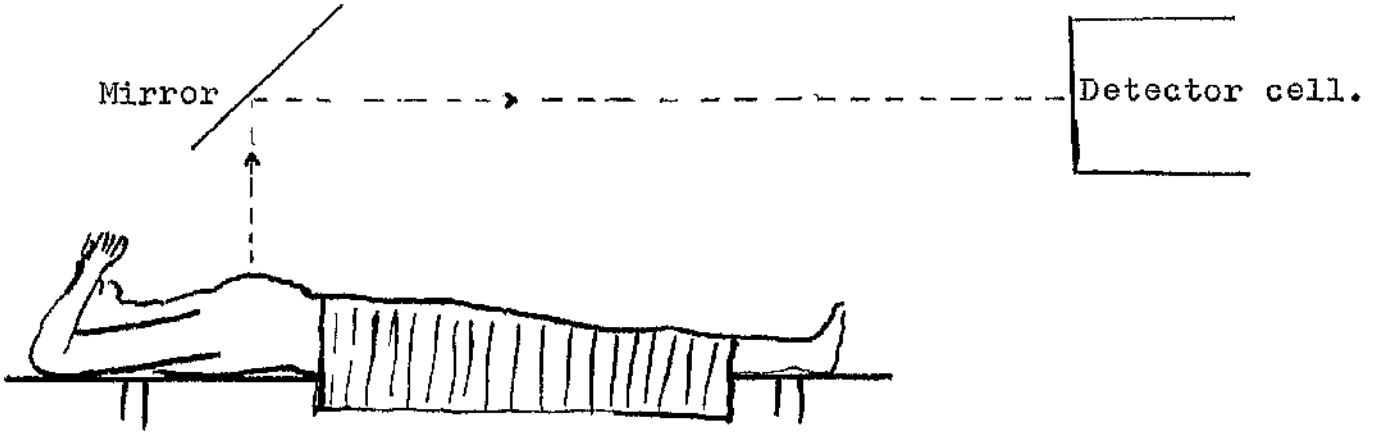


FIGURE 10.
Patient lying and using mirror.



In the thermography room I completed the medical details of the history. The thermographic scanning was done before the clinical examination in order that the examining hand did not warm up the breasts.

Those women in whom mammography was indicated, were given appointments to attend the Royal Victoria Infirmary. The majority of appointments were the following day or, at most, within forty-eight hours.

Each week Dr. Hacking and I had a conference to correlate clinical findings, thermograms and mammograms, before deciding the recommendations in each case.

Phase II of the survey lasted for twenty-one months and during that time 3,684 women were seen.

Phase III

This consisted of a highly selected group of women, mainly chosen from those attending during Phase II. This group was considered to be at high risk and comprised

(1) all those with equivocal thermograms, with or without doubtful mammograms from Phase II

(2) women with knotty, fibrocystic breasts or nipple discharge, from Phase II

(3) previous history of a benign lesion

(4) those with family history of breast cancer

(5) childless women and those of low parity

(6) women with a late menopause

(7) women with a past history of endometrial cancer

From January to December, 1969, by which time women under thirty five years of age were excluded from Phase 11, 66.8% of the otherwise unselected women qualified to be included in Phase 111.

My reasons for considering such women to be a high risk are as follows:-

Dysplasia

The literature on the relationship of breast dysplasia and cancer is highly conflicting. Bloodgood, in 1929 (81) was not impressed with the possibility, and Campbell, in 1934 (82) reported on a group of two hundred and ninety women with cystic disease. He followed them for times varying from two to fourteen years, and gives an incidence of 0.7% who developed carcinoma. Many other reports in more recent years (Clagett, 1944 (83), Lewison, 1953 (84), Kiar, 1954 (85), Davis, 1964 (86), Leis, 1964 (87), Veronesi, 1968 (88)) indicate that women with dysplasia have a three to

ten fold increased risk of developing carcinoma.

The great variation in these figures may be due to:-

(a) the wide spectrum of dysplasia

(b) differing interpretations of it

(c) the fact that in some series the diagnosis was made clinically and in others histologically, and

(d) the varying length of follow-up time - Campbell two years; Kiar an average of seventeen years

Although the clinical correlation is not conclusive, the relationship appears to be more than fortuitous; there is undoubtedly a link between histologically proven dysplasia, especially epithelial hyperplasia of the large ducts, and carcinoma (Humphrey (89), Rush (90) and Kern (91)).

Previous Biopsy for Benign Lesion

Shapiro (92) comments that women who have had previous benign conditions - lumps, cysts or abscesses, are at increased risk. The work of Potter (93) would appear to support this.

Family History

As said previously, this is a familial disease, (Morse (77),

Wynder (94), Dunn (76), Anderson (78), Penrose (95)). All these workers support this concept, those at greatest risk being the daughters and sister of victims.

Wynder considers that, apart from a previous breast cancer, a history of the disease in the immediate family is the greatest risk factor.

Marital Status and Parity

The earliest recorded observation of the relationship of the unmarried state and breast cancer appears to be by Ramazzini in 1713 (96). Shapiro's present survey in New York (92) confirms that this cancer is commonest in umarried nullipara. Wynder (94) found a two fold increased risk in all nullipara, unmarried or married. It has been suggested that (97, 96) the woman who first starts child bearing after the age of thirty years is at greater risk of breast cancer than a woman of the same age and parity, but who had her first pregnancy before the age of twenty. (Although age at first pregnancy was noted, it has not been taken into account when assessing the risk factors).

Late Menopause

Several workers (Wynder (98), Shapiro (92), Levin (99)) have published figures indicating that women with prolonged menstrual

activity, i.e., menopause occurring after fifty years of age, have an increased risk of breast cancer. Olch (100) found that seventy two percent of a control group of women had ceased to menstruate by age fifty, whereas only fifty five percent of breast cancer victims were post-menopausal at age fifty.

Conversely, an early artificial menopause appears to confer some immunity to breast cancer (101, 92, 102) and Feinleib (102) also states that bilateral oopherectomy before age forty years reduced the risk of breast cancer by seventy five percent; women with an early menopause were not excluded if there was another risk factor.

Endometrial Cancer

MacMahon (103) and Bailer (104) have published series indicating that women with endometrial cancer run a thirty to fifty percent greater risk of developing breast cancer. From my own experience of long term follow up of gynaecological cancer patients, I have seen several women with two separate primaries - in endometrium and in breast. These two cancers are hormone dependant and could have a common aetiological factor, probably pituitary.

Race, lack of breast feeding and social class have also been cited in the epidemiology of breast cancer but I have not included these factors in my high-risk group.

The incidence of breast cancer is very low in the Japanese (105, 98) and high in Jewesses (97). There were no Japanese in my unselected group and very few Jewesses.

Investigations in Europe and America have not confirmed the association of breast cancer and lack of breast feeding (106, 99); also with the overwhelming trend away from breast feeding there has not been a corresponding increase in the incidence of breast cancer.

The original interest in a relationship of breast cancer and lactation arose in Japan where lactation is normally prolonged but the incidence of breast cancer is low.

The peak incidence of breast cancer occurs in women of higher socio-economic class (107, 108). According to the Royal Statistical Society's classification, the women in my unselected group of Phase II were predominantly from the upper classes so that no further selection by this factor was required. This is a common finding in screening programmes, participants almost invariably being from the better educated group.

TABLE NO. I

Socio-Economic Class of Unselected Group		
I	Higher Professional and Managerial	29%
II	Other professions Higher Clerical and Supervisory	20%
III	Skilled Tradesmen Clerks	43%
IV	Unskilled Workers	7%
V	Social Pensioners	1%

During Phase III the women are again seen by appointment only, but only twelve appointments are made per session now. This is for the following reasons:-

(1) Most of the women have attended at least once before, and their previous thermograms have to be compared with the current findings. This prolongs the time in the Thermograph Room.

(2) All patients have senography done.

One highly trained radiographer with a dark room technician can cope with twelve women per session. This is in contrast to mammography by conventional methods - by which only five women could be done per session.

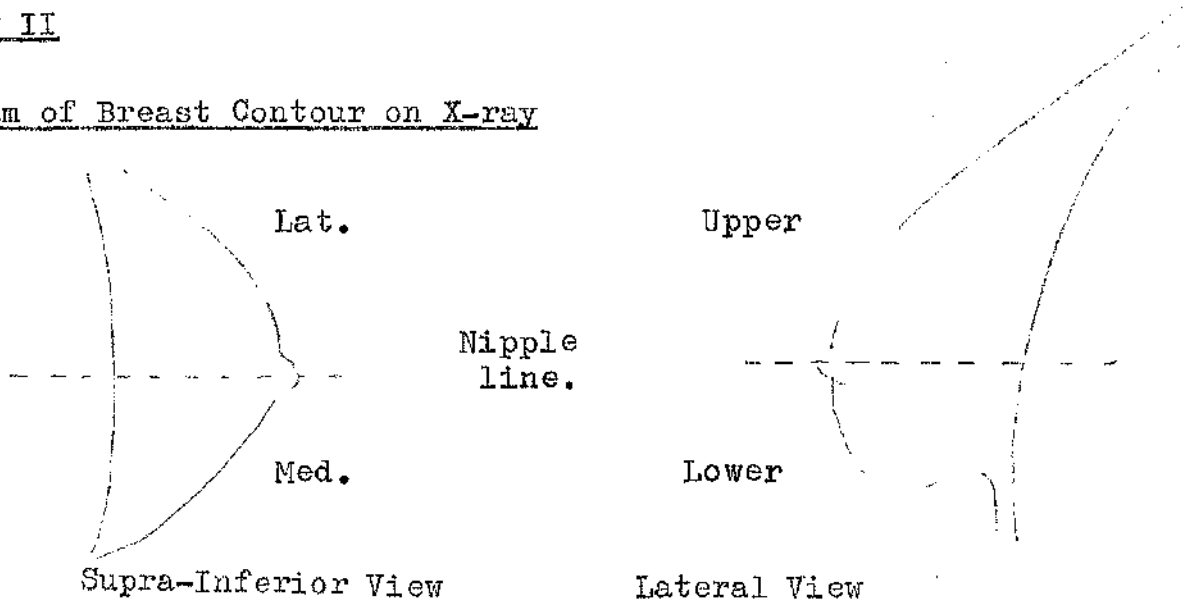
The screening of women in the high-risk category continues but this thesis is limited to a review of the work done between January and July, 1970. This limited time was chosen in order to ensure a follow-up period of at least twelve months to allow some time for discovering false negatives.

The Biopsy

When a lesion is discovered on thermography and mammography, and is impalpable, choice of the biopsy site may be difficult. As has already been discussed, there need not be spatial relationship between the hot spot on the thermogram and the lesion. The breast is an extremely labile organ, especially in the older woman. Frequently, there is little similarity in contour between the breast as it appears in the two views on mammography and the breast of the woman lying on the operating table.

FIGURE II

Diagram of Breast Contour on X-ray



From the mammogram, the surgeon is given a guide as to the distance of the lesion above or below the nipple and medial or lateral to it. Skin marking with lead shot on the mammogram was considered but was of very little help in the very lax breast, which was the greatest problem.

It is known that, during Phase II, the lesion was probably missed on biopsy in two women.

CASE HISTORY

Mrs. A.	Aged fifty six	3 years post-menopausal
June 1969	No palpable abnormality in moderate sized breasts	
	Thermography	Right 1.5° differential upper outer quadrant Left very vascular compared to right
		Opinion: Bilateral abnormal thermograms
	Mammography	Bilateral calcification of punctate nature suggesting malignancy
	Bilateral biopsies of suspect area	
	Histology	Marked epitheliosis

March 1970 No palpable findings

Thermography Right Very vascular outer half
Left 2° differential upper outer

Senography Bilateral areas of punctate calcification

Opinion: Bilateral carcinoma

Bilateral biopsies revealed: multifocal carcinoma

The possibilities are that:-

(a) the correct area was not removed for histological examination

(b) that insufficient sections were cut from the specimen

(c) that the epitheliosis was the cause of the original thermographic and mammographic findings and subsequently underwent malignant change

The case history of Mrs. U.B. was similar (ref. Table No. 19).

When the senograph was acquired, this major problem of the biopsy site was greatly simplified. The routine is now as follows:

The biopsy site is decided as before. I X-ray the specimen immediately, the wound being kept open meanwhile. It takes about fifteen minutes to radiograph the biopsy, to compare it with the mammogram and send a message back to Theatre, confirming, or not,

that the correct area is included in the biopsy specimen.

The specimen is then sliced and re-X-rayed, in order to select the block of tissue most involved for priority processing in the Histological Department (Plate No. 31). When this routine was first adopted, a further difficulty was experienced on slicing the biopsy. The slices on X-ray appeared to contain more scattered calcification than the original X-ray of the whole biopsy specimen. It was discovered that it was possible to transfer spicules of calcium from a cut surface, via the knife and the cone of the senograph. Great care is now taken to avoid this. Between each slice, the knife is washed thoroughly and dried, as is the lower surface of the cone between each radiograph; the specimen is cut on waxed paper and transferred to the X-ray film packet on this, a fresh paper being used for each slice.

The tissue for histological examination is fixed in Sousa Solution; this preserves nuclear detail much better than formalin and in work of this nature, nuclear detail is most important. Between fifteen and thirty sections are examined from each specimen.

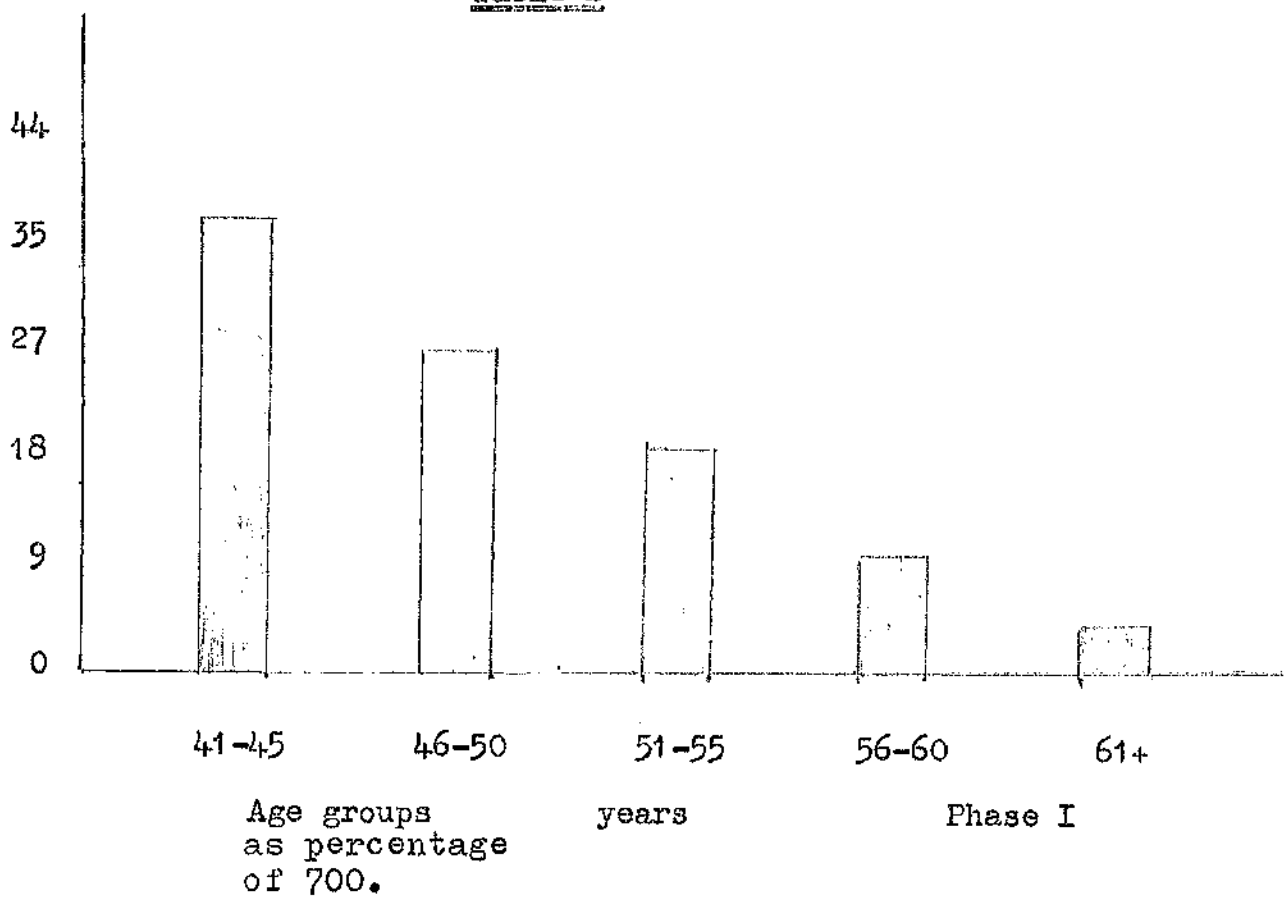
The frozen section technique is of no value when dealing with lesions as small as the impalpable cancers, diagnosed by thermography and mammography.

RESULTS

Phase I

Of the seven hundred women, whose age groups are shown in Table 2, eighty five percent were considered, on clinical examination, to have normal breasts.

Table 2



The other one hundred and seven, i.e., fifteen percent, had various clinical findings as shown in Table 3 and were referred to Dr. Hacking formammography.

Table 3

PATIENTS REFERRED FOR MAMMOGRAPHY 107				
	Clinical Diagnosis	Mammography Report	Histology	Follow up (in years)
1	Carcinoma 6 cm in size with palpable axillary glands	Scirrhous carcinoma	Scirrhous cancer 14 nodes examined - 3 involved	Alive & well at 33/12
1	Possible cancer on account of skin dimpling. No mass	0.5 cm intraduct cancer	Intraduct Cancer. Nodes negative	Alive & well at 47/12
1	Fibroadenoma	Fibro-adenoma	Cancer. Biopsy delayed for 12/12	Died 18/12
104	Generally knotty	Dysplasia	-	Offered appointments for Phase II 54% accepted

The woman considered to have a fibroadenoma refused biopsy as she was about to leave the district. Eighteen months later she died of breast cancer with widespread metastases.

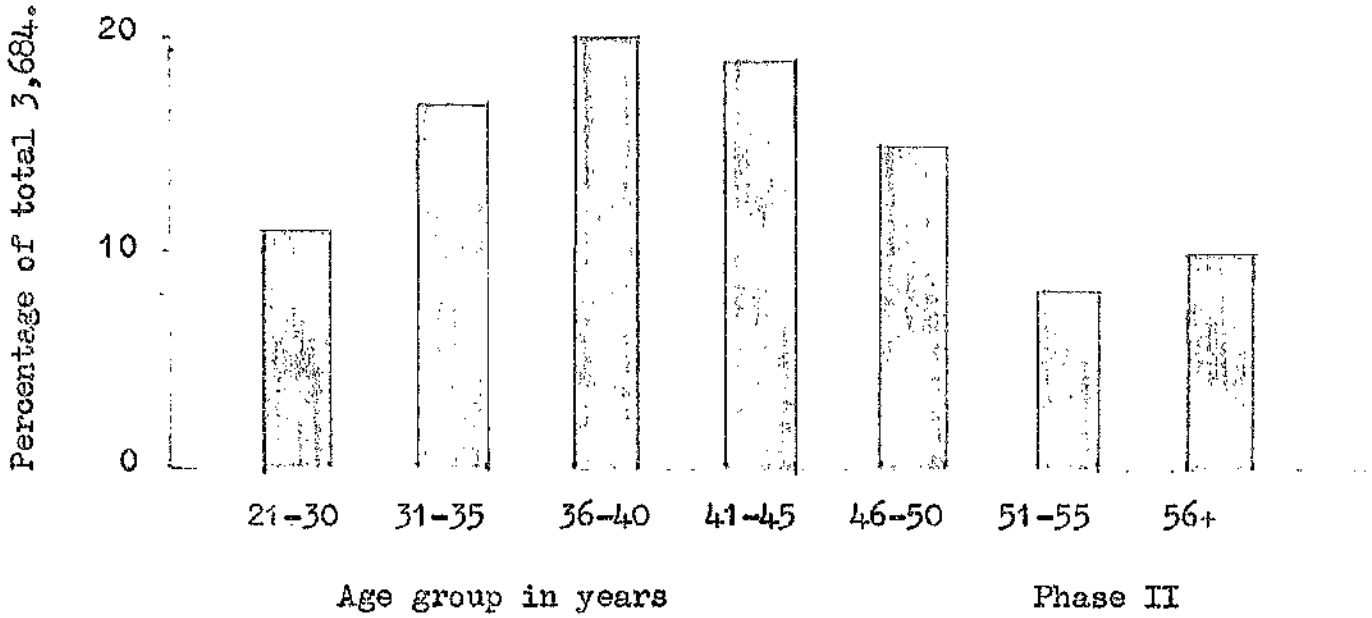
No active effort has been made to follow up the normal women in Phase I, as this was not the object of this survey.

By means of clinical examination, with mammography in selected women, this is a pick up rate of two in seven hundred, only one of which was confined to the breast, i.e., this is a pick up rate for Stage I breast cancer of 1.4 per thousand, which is considered to be quite adequate.

Phase II

There were 3,684 women in this group. Their age groupings are as in Table No. 4.

Table 4



One thousand and twenty or 27.7% of this unselected group were aged thirty five or younger. Three of the women with fibroadenomata (see Table 9) were in this group.

Thermogram Patterns

The thermogram patterns were classified into four groups:- avascular, vascular, very vascular & mottled.

TABLE No 5

THERMOGRAM PATTERNS	
Pattern	% of Total
Avascular	25%
Vascular	53%
Very Vascular	12%
Mottled	10%

All patterns were found in all age groups. A majority of post-menopausal women have cold avascular breasts; in the women who have been screened before and after the menopause, over a three year period of time, it has been noted that many show a lessening of the vascular pattern.

The most difficult patterns to interpret were the highly vascular and the mottled patterns, particularly in the pre-menstrual week. A negative report in these patterns was made only when the breasts were strictly symmetrical, and in sixty six women only after the test had been repeated between the seventh to tenth day of the menstrual cycle. Women, in whom the diagnosis of fibrocystic disease was made on mammography, had asymmetrical vascular or mottled thermogram patterns. I feel that the mottled pattern may indicate epitheliosis. In those women with a histological report of epitheliosis on biopsy, eighty percent had a mottled pattern; however, many women with a mottled pattern have not come to biopsy. They have,

however, been included in the follow-up group and three have later developed a hot spot and a positive mammogram, revealing four cancers.

Case History

Mrs. A.A.	Aged sixty	Fourteen years post-menopausal
	March 1969	Clinically normal, breasts moderate size, but fatty
		Thermogram negative, mottled pattern
	April 1970	Clinically normal
		Thermogram Left: 3° temperature differential and more vascular
		Mammogram Left: increased vascularity
	July 1970	Clinically normal
		Thermogram: Left: 4° differential
		Senogram Left: Ill-defined opacity, biopsy advised
		Histology Scirrhous carcinoma

When women return to the Unit for annual review, the constancy of the individual thermal pattern is most impressive in normal women, even when there has been a pregnancy in the interval. Recently I have re-screened three women, all of whom have had a full time pregnancy between the first and most recent screening. Their thermal patterns

were comparable with the films taken 24, 30 and 35 months before. Only one of the babies was breast fed - for four months, ending seven months before the date of re-screening.

I consider that any change from a patient's own basic pattern of thermogram is of diagnostic significance.

Size of Breasts

On clinical examination, breasts were assigned to one of four groups, according to size -- as Table 6.

Table 6

Size of Breast	% of Total
Small	25%
Medium	46%
Medium but pendulous	13%
Large and pendulous	16%

No relationship was found between type of thermogram pattern and size of breast. My fear that the pendulous breast would give

a false negative thermogram has not occurred in spite of the difficulties of cooling the infra-mammary area, and of the fact that there is such a high proportion of fat in many pendulous breasts, especially if they are large.

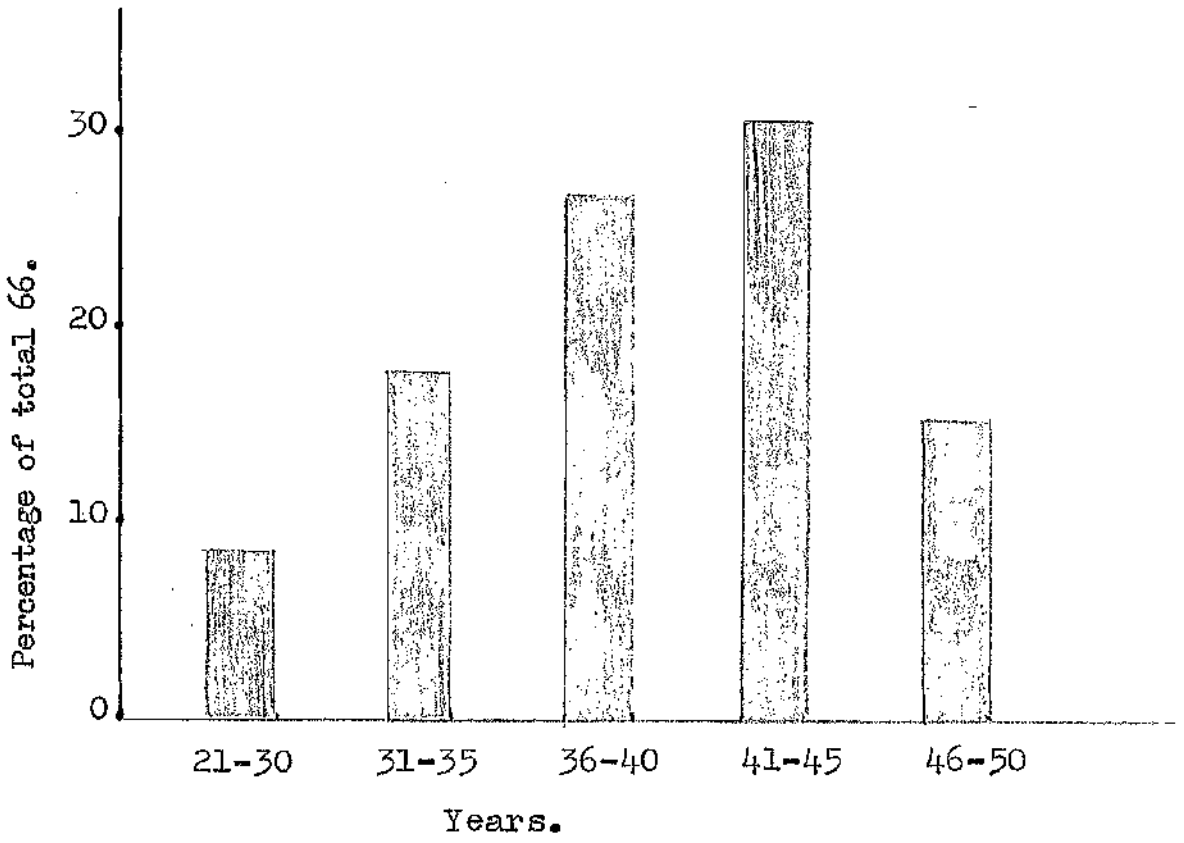
Phase II

Table 7

Total number of women examined				3684
Suspicious thermograms on first visit			471 (12.8%)	
Highly vascular pattern, repeated at different stage of menstrual cycle and considered negative		66		
Number referred for mammography		405 (10.9%)		
Mammograms negative	141			
Mammograms, abnormal, but negative for malignancy	169			
Fibrocystic disease 144 Duct ectasia 16 Multiple cysts 1 Fibroadenoma 6 Resolving abscess 1 Resolving haematoma 1				
Mammograms, positive for malignancy	32			
Mammograms, suspicious for malignancy, for follow-up 6/12	56			
Patients unsuitable for mammography	7			
due to youth 1 smallness of breast 6				

Table 8.

Age groups of 66 women with doubtful thermograms, repeated at different stage of the cycle, considered negative.



Among the group of 141 women with thermograms considered to be abnormal, but whose mammograms were negative, are twenty five women whom I now believe to have anatomical aberrations, i.e., the venous patterns of the two breasts are markedly different and have remained constant on repeated thermography over a three year period. There has never been a palpable abnormality and X-ray has remained normal. This gives an incidence of anatomical aberration of 25 in 3684 or 0.7%. (Plate XIV)

Phase II Biopsies

During Phase II, sixty one patients had breast biopsies performed, fifty six of these in our own Unit. There were two main groups

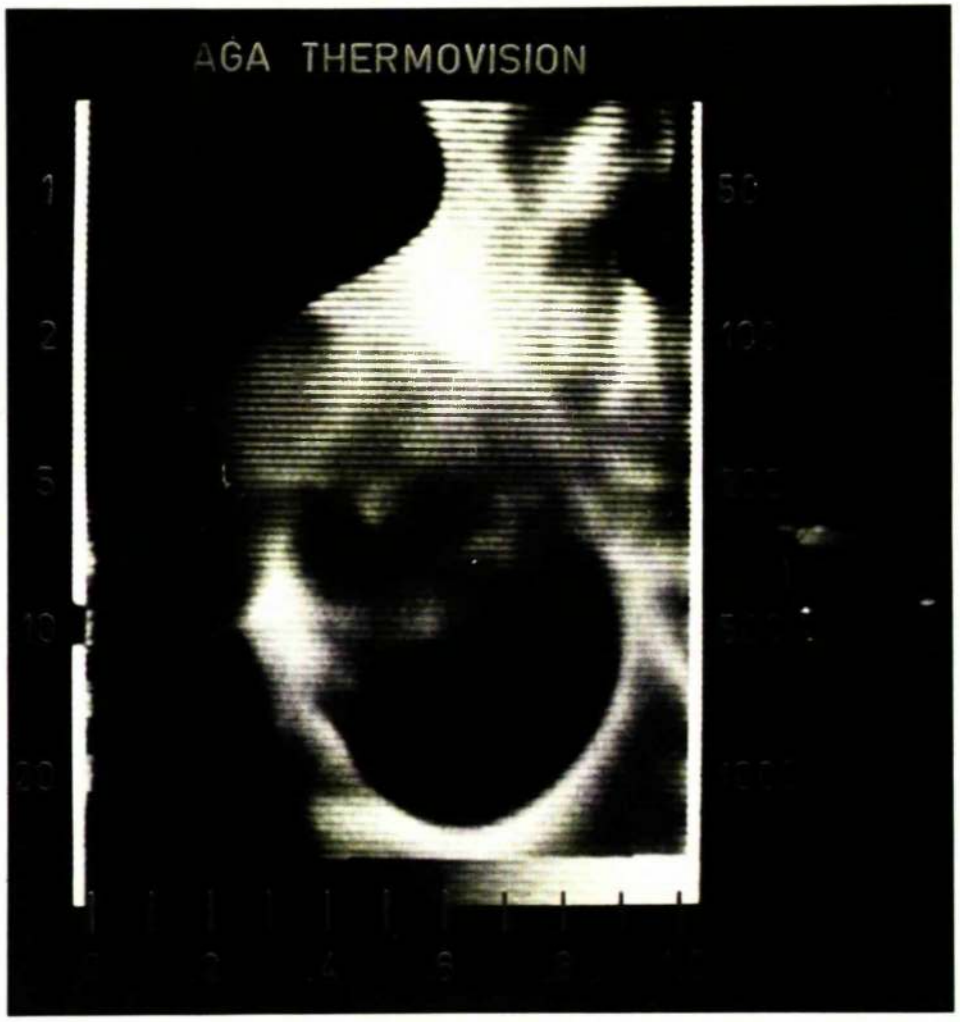
A. Biopsy indicated by clinical finding (Table 9)

B. Biopsy indicated on thermography and/or mammography, in the absence of clinical abnormalities (Table 10)

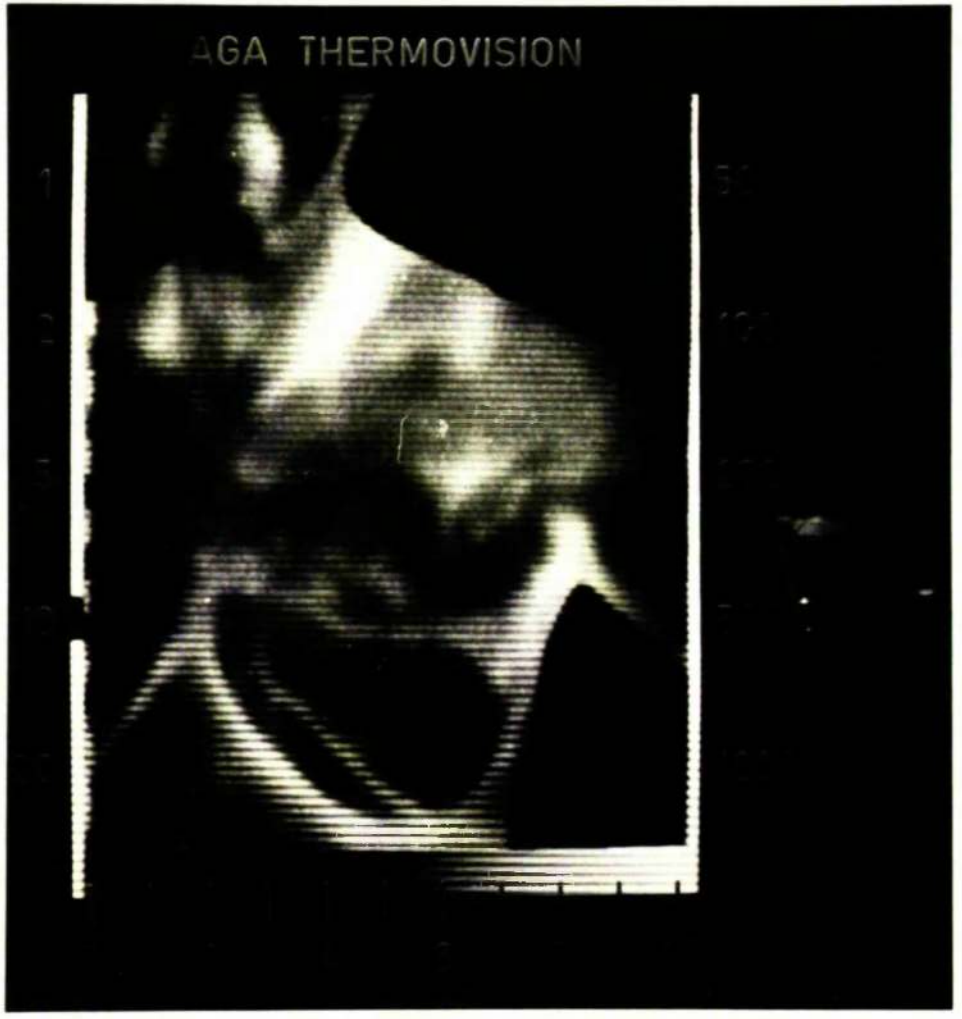
Eleven patients did not have mammography done, the reason being the smallness of the breasts in nine women; the other two women were aged nineteen and twenty years with a fibroadenoma on clinical examination. It is known that there is insufficient contrast on X-ray in the young breast to give any help in the diagnosis (109).

Plate X1V.

Right oblique.



Left oblique.



Abnormal thermogram. - due to aberrant venous pattern; this woman has no clinical findings, a constant thermogram and a normal X-ray over thirty months.

Thirty nine (83%) of the forty eight breasts with histologically benign lesions had abnormal thermograms. This confirms the statement made earlier that temperature increases or an area of increased vascularity in the breast as noted on a thermogram, are not specific to malignancy but occur with any increase in cellular activity.

Eleven patients with palpable lesions had normal thermograms. Five of these were simple cysts, two very fibrotic fibroadenomata, and one a lipoma - all lesions of low cellular activity; in two others, the histology showed adenosis and cystic disease. The one carcinoma with a negative (i.e., false negative) thermogram was a large scirrhous tumour with much fibrosis in a small breast, and presumably was of low biological activity at the time of examination by thermography.

The degree of temperature differential is not helpful in indicating a benign or a malignant lesion. The proven cancers had temperature differentials varying between nil (in the false negative) to 4°, with an average differential in the abnormal thermograms of 3°. In the benign lesions, the variation was between 1.5° and 4°.

In normal women, I have found that 92% of left breasts are $\frac{1}{2}$ to 1° warmer than the right breasts; this is a diffuse warmth.

I have no explanation to offer for this, but it results in a temperature differential in the right breast being even more significant.

Of the 405 mammograms done, there was a false positive rate of 5.4%. Two considered negative at first biopsy (Table 19, Cases No. 24 and 31) had repeated biopsies ten months and nine months later, at which time the histological reports confirmed the presence of cancer.

It is known that six patients developed clinical cancer following negative clinical examination and a negative thermogram; details of these are given in Table 11.

Four of these cancers developed within twelve months and must be considered false negatives, i.e., a false negative rate for clinical examination and thermography of 0.11%. The other two developed in women who had defaulted from the annual follow-up appointment.

The pick up rate for breast cancer in the 3,684 women examined clinically, and by thermography, with mammography by conventional methods in 10.9%, was two clinical cancers and nine

pre-clinical asymptomatic cancers. (Pick up for pre-clinical cancer 2.44 per thousand).

If the 1020 women under 35 years were excluded, as in most screening programmes, this would make the pick up rate 3.4 per thousand.

TABLE 9 Phase II

A. Biopsy indicated by clinical findings

	Clinical Opinion	Thermogram	Mammogram	Histology
1	Benign cyst	Normal	Not done	Cyst - benign
2	Benign cyst	"	" "	" "
3	Benign Cyst	"	" "	" "
4	Benign Mass	Normal	Benign Opacity	Fibroadenoma
5	Benign Cyst	"	" "	Benign cyst
6	Benign Cyst	"	" "	Benign cyst
7	Benign Cyst	"	" "	Lipoma
8	Nodule ? Carcinoma	Normal	Suspicious	Fibroadenoma
9	Nodule ? Carcinoma	"	Benign op.	Sclerosing adenosis
10	Benign Mass	"	" "	Cystic disease
11	Benign cyst	Abnorm. Vasc. +++	Not done	Intracystic carcinoma
12	Benign cyst	Abnorm. Mottled Vasc. ++	" "	Epitheliosis

13	Benign Cyst	Abnormal	Vasc. ++	Not done	Cystic Disease
14	Benign cyst	"	2°	" "	" "
15	Benign cyst	"	4°	" "	Papillomatosis
16	Benign mass	"	Vasc. ++	" "	Fibroadenoma
17	Benign mass	"	2°	" "	Fibroadenoma
18	Benign mass	"	4°	" "	Fibroadenoma
19	Benign mass	"	Vasc. ++	" "	Epitheliosis
20	Benign Mass	Abnormal	2°	Benign Opacity	Fibroadenoma
21	Benign mass		Vasc. ++	"	Fibroadenoma
22	Benign mass		Vasc. ++	"	Fibroadenoma
23	Benign mass		1.5°	"	Cystic Disease
24	Benign mass		2°	"	Cystic Disease
25	Benign mass		3°	"	Adenosis
26	Benign Mass	Abnormal	2°	Fibrocystic Disease	Epitheliosis
27	Benign mass		Vasc. ++	"	Cystic Disease
28	Benign mass		3°	"	Cystic Disease

29	Benign mass	2°	Fibrocystic Disease	Epitheliosis
30	Clinical Cancer	Normal	Skin thickening only	Scirrhous Carcinoma
31	Clinical Cancer	Abnormal 4°	Cancer	Adenocarcinoma
32	Clinical Cancer	Abnormal Vasc. ++	Cancer	Chronic abscess
33	Clinical Cancer	" " 2°	Cancer	Adenosis
34	Clinical Cancer	" " 2°	Calcified fibroadenoma and 5 mm focus of cancer	Confirmed X-ray report
x	8, 9, 10	These women had knotty breasts with a dominant mass		

TABLE 10 Phase II

B. Biopsy indicated by Thermogram and/or Mammogram

	Clinical Opinion	Thermogram	Mammogram	Histology
1	Generally knotty	Abnormal 3° C	Positive area	Cystic Disease
2	Generally knotty	Vasc. ++ 2° C		"
3	Generally knotty	2° C		Negative
4	Generally knotty	2.5° C		Cystic Disease
5	Generally knotty	3° C		Carcinoma
6	Generally knotty	4° C		Carcinoma
7	Generally knotty	Mottled 3.5°		Adenosis
8	Generally knotty	" 4°		Epitheliosis
9	Normal	Abnormal Vasc. ++ > 4° hot spot	Defaulted	4/12 later carcinoma
10	Normal	Abnormal 2° C	Positive area	Carcinoma
11	"	" Vasc. ++	" "	"
12	"	3° C	" "	"
13	"	2.5° C	" "	"
14	"	2.5° C	" "	"
15	"	3.5° C	Spiculated op.	"

16	Normal	Abnormal 4° C	Positive area	Epitheliosis
17	"	" 3° C	" "	"
18	"	" Vasc. ++	" "	Cystic disease
19	"	" 1.5° C	" "	" "
20	"	" Vasc. ++	" "	" "
21	"	" Vasc. ++	" "	" "
22	"	" 4° C	" "	" "
23	"	" 2.5° C	" "	" "
24	"	" 3.5° C	" "	" "
25	"	Abnormal Mottled 2° C	" "	Epitheliosis
26	"	Abnormal Mottled 3° C	" "	"
27	"	Abnormal Mottled 1.5°	" "	Sclerosing adenosis

Details of False Negatives in Phase II

Table 11

	Age	Family History	Parity	Clinical Details	Thermogram	Mammogram	*Latent Period	Reason for Seeking Advice	Histology	Treatment
Miss M.M. 1.	40	-	0	Normal Moderate Size	Negative Vascular	Not done	16/12	Nipple retraction Defaulted follow up	Adenocarcinoma Stage I Nodes Negative	Modified Radical Mastectomy X-ray Therapy
Mrs. M.O. 2.	42	-	1	Normal Moderate Size On Lyndiol till 3/52 ago	Negative Highly Vascular	Not done	9/12	Felt nodule	Florid Epitheliosis & lobular carcinoma in situ	Simple Mastectomy
Mrs. S.J. 3.	35	-	3	Generally knotty, especially Left. On Ovulen. Large, fat.	Negative Vascular	Not done	8/52	Lump in axilla	Carcinoma Left axillary tail, & gland in axilla	Lymphadenectomy & X-ray Therapy
Miss M.S. 4.	56	Aunt	0	Normal Post-menop. Five years Moderate.	Negative Avascular	Not done	22/12	Defaulted annual follow up. Felt lump - thought by surgeon to be fibroadenoma.	Anaplastic carcinoma Stage I Nodes negative	Radical Mastectomy
Mrs. D.S. 5.	45	-	0	Mildly knotty Moderate	Negative Vascular 1° differential left.	Not done	9/12	Felt lump - thought by surgeon to be cyst in fibro-cystic breasts	Intraduct carcinoma Stage I Nodes negative	Modified Radical Mastectomy
Mrs. K.M. 6.	63	Mother aged 35	0	November, 1968 Normal Small November, 1969 Normal	Negative Avascular Negative	Not done Not done	 10/52	 Pain in breast	Feb. 70 R. Scirrhous ca. 1.5 x 2 cm. L. Three foci of scirrhous ca. 2.5 x 2 cm., 1.5 x 2 cm., and 1 x 1 cm.	Treatment Bilateral Simple Mastectomy

*Latent period - time interval between negative thermogram and occurrence of symptoms. All thermograms have been reviewed. In the case of Mrs. D.S., (No. 5), with considerably more experience now, I would consider the thermogram sufficiently suspicious to warrant mammography.

All six patients consulted their family doctors when symptoms developed. They were referred to the nearest General Hospital and unfortunately, I did not have the opportunity to rethermogram them.

As a result of good liaison with colleagues throughout the region, I obtained details of all the cases.

RESULTS Phase III

Table No. 12

Follow up of Phase II in Phase III

Total number offered appointments January to July, 1970		1137
Number attended	1017	
Referred to Royal Marsden Hospital as now living in London area	3	
Killed in car accident	1	
Died - carcinoma ovary	1	
carcinoma large bowel	1	
+Left district, mainly gone abroad	22	
True defaulters	92	
Of the defaulters		
Positive family history	48	
Previous breast pathology (biopsy for benign condition)	31	
©Previous suspicious findings on thermogram and/or mammogram	13	

+Four of these women have attended recently; they requested appointments while in the district again to visit relatives.

©One of these women, who had a suspicious thermogram but a negative mammogram, had a radical mastectomy performed twenty-six months after the screening date. The cancer was limited to the

breast.

Of the 1017 women in Phase 111, 245 gave a family history of breast cancer, as detailed in Table 13.

TABLE 13

Details of Family History of Breast Cancer in Phase III

(Total number with family history 245)

Number in Group	Sister	Mother	Maternal			
			Aunt	Grand-mother	Great Aunt	Cousin
44	1					
8	1		1			
3	1	1				
1	1	1		1		
1	1	1	1	1		1
2	2					
1	2		1			
1	3	1	1	1		1
62		1				
9		1	1			
7		1		1		
2		1	1	1		
2		1				1
1		1	2			
1		1	1			6
46			1			
7			2			
4			1	1		
1			1	1	1	
1			2	1		
40				1		
1				1		1

TABLE 14

Marital Status and Parity	Total No. 1017	
Unmarried and nulliparous	53	5.2%
" para 1	2	0.2%
Married and nulliparous	129	12.7%
" para 1	240	23.6%
" " 2	372	36.6%
" " 3 or over	221	21.7%

TABLE 15

Menstrual Status	Total No. 1017	
Post menopausal	304	29.8%
Menopause artificial after aged 40	88	8.6%
Bilateral oopherectomy before age 40	16	1.5%
Menopausal	81	7.9%
Menopause after age 50	74	7.2%

TABLE 16

Incidence of previous benign breast condition in 1017			
A.	History of benign condition		192
	1.	Biopsy before initial screening	126
	2.	Biopsy during Phase II	22
	3.	Abscess incised	39
	4.	Nipple discharge	5
B.	Findings in Phase II		440
	1.	Uniformly knotty on palpation thermogram negative	207
	2.	Uniformly knotty on palpation thermogram suspicious, memmogram negative	89
	3.	Uniformly knotty on palpation, thermogram suspicious, mammogram fibrocystic disease	144

Some patients occur in groups A. & B.

TABLE 17

Follow up during Phase III of women in Phase II with abnormal thermograms and suspicious mammograms (Repeat X-ray examination by Senograph)

Total number of women		56
Lost to follow up	4	
Left district	2	
"Frightened to come"	1	
Lost	1	
Senogram, abnormal but negative for malignancy	20	
Fibrocystic disease	8	
Duct ectasia	2	
Benign calcification	6	
Resolving haematoma (observed over 18/12)	1	
Benign opacity, now palpable & biopsied	3	
D.H. Histology - Simple cyst		
P.B. - Cystic disease		
J.C. - Severe adenosis		
Senogram negative	20	
Senogram progressive lesion no palpable lesion	11	
Biopsy reports		
F.H. Bilateral carcinoma (Right negative therm)		
E.W. Cystic disease		
E.P. Bilateral carcinoma		
A.L. Sclerosing adenosis		
A.H. Epitheliosis		
L.McL. Fat necrosis		
A.P. Adenosis		
D.S. Intraduct pappillomatosis		
M.B. Carcinoma		
A.B. Lobular in-situ carcinoma		
J.B. Adenosis		
J.S. Remains suspicious but not progressive	1	

TABLE 18

Phase III

Total number of women examined			1017
Suspicious thermograms		250	
Suspicious thermograms associated with clinical or senographic features of malignancy	27		
"False positive" thermograms	223		
ABNORMAL SENOGRAMS		434	
Senograms, positive for malignancy - for biopsy (ref. Tables 19 & 20)	39		
Senograms, with suspicious features - for early follow up	87		
Doubtful calcification	32		
Unilateral increase in vascularity	27		
Asymmetrical duct pattern	11		
Vague opacity	17		
Senogram, abnormal, but negative for malignancy	301		
Fibrocystic disease	165		
Duct ectasia	46		
Multiple cysts	9		
Fibroadenoma	1		
Fibroadenoma (calcifying)	6		
Cyst	3		
Benign calcification	71		
Senograms, uniformly dense with no contrast, no report issued	7		

With reference to Table 7, no breasts were considered to be too small for senography, in contrast to mammography using conventional equipment. No young patients were seen in Phase III.

TABLE 19

Phase III

A. Biopsy indicated by clinical findings

	Clinical Opinion	Thermogram	Mammogram	Histology
W.W. 1.	May 69 Normal	L. Vasc. ++ upper outer	Fibrocystic disease	
	Feb 70 Nodule L. probably carcinoma	L. upper outer	Fibrocystic disease with punctate calcification L.	Normal tissue
S.L. 2.	Dec. 68 Normal Jan 70 Cyst L.	Negative Negative	Not done Fibrocystic disease with dominant cyst L.	Cystic disease
J.J. 3.	May 68 Normal May 69 Normal Apr 70 Cystic mass R.	Negative Negative Vasc. ++ R.	Not done Not done Cyst 34 x 38 mm. vague margin one point	Cystic disease with lobular in situ carcinoma
K.F. 4.	Generally knotty esp. R; blood-stained discharge R. Cytology - negative	Vasc. ++ R.	Bilateral duct ectasia	Duct hyperplasia
A.L. 5.	Nodule R. probably carcinoma	Vasc. ++ R.	Punctate calcification R.	Cystic disease

D.K. 6.	Nodule L; sero sanguineous discharge L. Cytology - neg.	Very vascular	Negative	Intra-duct papilloma.
B.P. 7.	Apr 69 Generally	L. 4°	Dense adenosis	
	Nov 69 No change	L. 1.5°	Dense adenosis	
	Mar 70 Knotty with dominant mass L. ? fibro-adenoma	L. 1.5°	Adenosis with lobulated opacity in L.	Fibroadenoma
D.P. 8.	Cyst L.	L. 1° areola	L. Cyst 25 x 10 mm	Cyst
J.H. 9,	Mar 69 Knotty generally	L. upper outer 1° Very vasc. pattern	Not done	
	Oct 69 No change	L. 4°	Bilateral duct ectasia	
	Jan 70 Generally knotty, dominant nodule R. areola	Very vascular pattern symmetrical	Bilateral duct ectasia with opacity R - ? neoplasm	Cystic
K.E. 10.	June 69 Normal	R. 1.5° in avasc. pattern	R. Negative L. Vague opacity	
	Jan 70 Nodule L.	R. No change L. Increased vascularity	R. Negative L. Punctate calcification	L. Lobular in situ carcinoma

M.W. 11.	June 69	Normal	Mottled pattern L. 3°	Not done	
	Sept 69	Normal	R. 2.5°	L. increased vascularity	
	Apr 70	Normal	Mottled pattern R. 2.5° areola L. upper outer 1.5°	No change	
	Nov. 70	Discharge serous, bilateral. Cytology R: no cells L: Many appearing cells	No change	No change	L. Severe papillomatosis
E.I. 12.	Jan 70	Possible cyst in large pendulous left breast	Negative	Not done	
	Feb 70	No change	L. 1.5°	Cyst L. with increased vasc.	Cystic disease
V.B. 13.	May 68	Knotty	Normal	Not done	
	Jan. 70	R. Nodule probably carcinoma L. knotty	R. Vasc. ++ L. areola 2°	R. carcinoma L. suspicious calcification	R. Adeno-carcinoma L. Cystic disease

J.C. 14.	May 69	Normal	L. slightly more vascular	L. vague opacity	
	Feb 70	Nodule L. breast	Bilateral vasc. ++ L. 2	L. opacity probably fibroadenoma but also minimal punctate calcification	Fibroadenoma with extensive intra-duct papillomatosis and gross adenosis in all sections
	Dec 70	Nodule R.	Very vasc.	R. Cyst with fuzzy margin Could possibly be malignant.	Gross papillomatosis and adenosis. Very active breasts but no evidence of frank malignancy.

One further patient, with a cyst, had the cyst aspirated. The cyst was filled with air and the breast re-X-rayed to exclude an intracystic lesion. The aspirated fluid was examined cytologically and no malignant cells found.

(plates XXll to XXV.)

TABLE 20

Phase III

B. Biopsy indicated by Thermogram and/or Senogram

	Clinical Opinion		Thermogram	Mammogram	Histology
M.B. 1.	June 69	Knotty generally	Vasc. pattern L. 4°	Bilateral localised punctate calcification - suspicious	
	Oct 69	No change	No change	No change	
	May 70	Knotty	R. Vasc. ++ L. 1°	Increase in calcification in R.	R. carcinoma
A.P. 2.	Feb 69	Normal	L. 2.5°	L. increased vasc.	
	July 69	Normal	L. 2° vasc. ++	No change	
	Mar 70	Normal	L. 2° vasc. ++	L. Punctate calcification	Adenosis +++
C.G. 3.	July 70	Normal	Mottled L. 5°	L. increased vasc. Group of suspicious calcification	Normal tissue (biopsy incl. calcification)
M.M. 4.	Oct. 69	Normal	L. 2°	L. Two calcification	
	Jan 70	Normal	L. 2° vasc. +++	Increase in group of calcification	Carcinoma
L.T.	Apr 69	Normal	Normal	Not done	
5.	May 70	Normal	Suspicious right upper inner and left upper outer	Right & left multifocal calcification suggesting carcinoma	Bilateral carcinoma

J.T. 6.	Oct 69	Generally knotty	L. vasc. ++ with 3°	Normal active breasts	
	Feb 70	Increase in knottiness in L.	No change	L. vasc. ++ Very dense breast tissue	L. Extreme epitheliosis
D.S. 7.	July 69	Knotty	Very vasc. pattern - no opinion	R. ill-defined opacity, probably not significant	
	Oct 69	Knotty	L. Susp. areolar area	Normal	
	Jan 70	Knotty discharge L. nipple Cytology - negative	L. Susp. due to asymmetry vascularity	L. Group of calcification rounded but vaguely suspect	Intra-duct papillomatosis
J.D. 8.	Feb 69	Very knotty	Negative	Not done	
	Sept 69	No change	L. slightly more vasc.	Not done	
	Jan 70	No change	L. Vasc. ++ 1°	L. Punctate calcification suggesting carcinoma	Minute scirrhous
F.H. 9.	July 69	Normal	L. Vasc. ++	L. - N.A.D. R. - Minimal calcification	
	Nov. 69	Normal	No change	No change	
	Mar 70	Normal	L. Vasc. ++ with 2°	L. Punctate calcification ++	L. Carcinoma
				R. Increase in punctate calcification	R. Carcinoma
D.M. 10.	Jan 70	Knotty generally	Very vascular pattern, no opinion	Fibrocystic disease with punctate calcification L.	L. Carcinoma

L.C. 11.	Oct 69	Normal	L. Vasc. ++	Not done	
	Feb 70	Normal	No change	L. group of suspect calcification	Lobular in situ carcinoma
C.M. 12.	Jan 69	Normal	Normal	Not done	
	Jan 70	Normal	L. Vasc. ++ 2.5°	L. Suspicious calcification	Papillomatosis and lobular in situ carcinoma
L.McL 13.	Sept 69	Normal	L. 3.5°	L. 7 mm opacity No malignant features	
	Mar 70	Normal	No change	Above opacity 12 mm well defined, probably benign	Fat necrosis
E.T. 14.	Apr 69	Normal	Mottled pattern	Not done	
	May 70	Normal	Mottled pattern	R. calcification suspicious of intra-duct carcinoma	Intra-duct carcinoma
D.T. 15.	Oct 68	Normal	Normal	Not done	
	Apr 70	Knotty	R. 2°	Bilateral adenosis. R. suspicious calcification	Adenosis

M.V. 16.	Apr 69	Knotty	R. 3.5°	Normal	
	Nov 69	No change	I.S.Q.	Not done	
	Feb. 70	no change	R. 2° and more vascular	R. Vasc. ++ Ill defined opacity	Adenosis
M.P. 17.	Mar 69	Normal	Normal	Not done	
	Apr 70	Normal	Normal	R. suspicious suggesting intra-duct carcinoma	Extensive sclerosing adenosis
L.S. 18.	Nov 69	Knotty L.	Normal	Not done	
	Feb 70	No change	L. Vasc. +	L. increased vascularity with cyst, appears benign	Cystic disease
H.F. 19.	Dec. 69	Knotty	L. Vasc. + 1δ	Not done	
	Feb 70	No change	L. Vasc. ++	L. Vasc. ++ and two calcification	
	July 70	No change	L. Vasc. +++ 2δ	L. Increase in calcification	Papillomatosis and sclerosing adenosis
C.G. 20.	Mar 68	Normal	Normal	Not done	
	Apr 69	Normal	Normal	Not done	
	July 70	Normal	L. Vasc. +++	L. Prominent duct pattern and punctate calcification	Adenosis and lobular in situ carcinoma

A.B. 21.	July 68	Cystic generally	R. 2.5°	Fibrocystic disease with vague opacity in R.	
	Sept. 68	No change	Normal	Not done	
	Jan. 69	No change	Normal	Fibrocystic disease	
	Mar 70	No change	L. Vasc. +++	L. calcification intra-duct carcinoma	L. lobular in situ carcinoma
R.S. 22.	Nov 69	Knotty	R. 3°	Very dense fibrocystic disease	
	May 70	No change	No change	Fibrocystic disease with suspicious calcification in left	L. Extreme sclerosing adenosis with very active cellular element
E.P. 23.	Oct 69	Normal	Vasc. pattern R. 1°	Bilateral minimal calcification	
	Dec 69	Normal	R. 3° Highly vasc. pattern	R. - minimal calcification L. - group of calcification suggesting carcinoma	R. Lobular in situ carcinoma L. Intra-duct carcinoma with early invasion
U.B. 24.	Feb 69	L. Nodule in knotty breasts	L. increased vascularity	Bilateral fibrocystic dysplasia	L. sclerosing adenosis
	Apr 70	Knotty	Bilateral great vascularity	Bilateral multiple foci of very suspect calcification	L. six foci of carcinoma R. multiple foci of several histological types

E.M. 25.	Mar 69	Knotty	Normal	Not done	
	Apr 70	No change	Normal avascular pattern	Bilateral dense adenosis R. Minimal calcification	
	Sept 70	No change	No change	Increase in calcification	Sclerosing adenosis and lobular in situ carcinoma
	(This was repeated on day of biopsy which had been delayed for family reasons)				
A.A. 26.	Mar 69	Normal	Mottled pattern	Not done	
	Apr 70	Normal	L. Vasc. ++ and 3°	L. increased vascularity	
	July 71	Normal	L. 4°	Ill-defined opacity	Carcinoma
J.D. 27.	Mar 69	Normal	Mottled pattern	Not done	
	May 70	Normal	Very vascular pattern - no opinion	L. area of calcification suggesting carcinoma R. small group suspect calcification	Bilateral carcinoma
M.M. 28.	Oct 69	Knotty	L. Vasc. ++ and 2°	Not done (too small)	
	Feb 70	No change	L. Vasc. ++ and 4°	L. punctate calcification	Carcinoma
C.H. 29.	May 69	Normal History of discharge R. nipple Nil obtained	Negative avascular pattern	Not done (too small)	
	Nov 69	No change	R. vasc. ++		
	Feb 70	No change	R. Vasc. ++	R. Opacity 20 x 26 mm ill defined	R. No frank carcinoma but very

			one point	active adenosis with mitotic figures Watch carefully
E.A. 30.	June 69 Normal	R. 4°	Group highly suspicious calcification	Epitheliosis
	Mar 70 Normal	R. & L. much more vascular and abnormal compared to June 69	Bilateral highly suspicious calcification	Bilateral carcinoma
E.T. 31.	Oct 69 Knotty	R_0 Vasc. + 1°	Not done	
	Jan 70 No change	No change	Vague opacity R.	R. considerable adenosis
D.S. 32.	May 69 Normal	Negative - avascular	Not done	
	June 70 Normal	R - vascular pattern L. - avascular	L. group of highly suspicious punctate calcification	Intra-duct papillomatosis very extensive. In one section is an area suspicious but not conclusive of malignancy
J.F. 33.	R. Normal	R. 3° R. upper outer	R. Minimal punctate calcification	Carcinoma R.
	(This was a biopsy in left breast)	done in a patient with a clinical carcinoma		
J.R. 34.	June70 L. normal	Suspicious round areola - vasc. ++	Suspicious calcification in dense area	Papillary adenocarcinoma
	(This was a biopsy in right breast)	done in a patient with a clinical carcinoma		

Phase III Biopsies

During Phase III, fifty patients had breast biopsies done, forty eight of these in our own Unit. Two were performed by surgeons in hospitals ten miles and twenty-two miles away; the specimens were sent to me for X-ray and preparation for histology. The biopsy material unfixed and wrapped in saline swabs and polythene, was conveyed by taxi.

As in Phase II, there were two groups:

A. Biopsy indicated by clinical findings (Table 19)

B. Biopsy indicated by thermography and/or senography, in the absence of clinical findings. (Table 20)

Of the twelve patients with palpable findings in Group A, three had negative thermograms. All three had cysts (lesions of low biological activity).

Three patients had carcinoma. All had suspicious thermograms; on senography, two were considered to be malignant and one suspicious of malignancy.

Carcinoma was suspected erroneously by all three modalities in two cases.

In Group B, there were twenty four carcinomas, confirmed histologically, in nineteen women. Fifteen of these were suspected on thermography before senography. Three were unequivocally negative on thermography and one negative but with a mottled pattern. Of the other five carcinomas, two women with bilateral lesions had highly vascular patterns with no temperature differential; the third had a highly vascular pattern and a unilateral lesion.

If these women had been screened by the routine of Phase II, at least three of the cancers would have been missed, as mammography was not done in women with negative thermograms and no clinical findings.

During a follow-up time, varying between eleven and seventeen months, one cancer is known to have been diagnosed in a woman with no evidence of cancer at the time of screening. The patient felt a lump and consulted her family doctor. The details are as follows:

Mrs. E.S. aged forty five years.

Married at twenty two years, two children aged twenty one and seventeen, the mother being aged twenty four when first child born.
Two years post-menopausal.

Family History: Paternal aunt, mastectomy aged sixty, died aged sixty one years.

13.5.69

Clinical examination: Moderate sized breasts
no abnormality

Thermography negative

10.6.70

Clinical examination:	Generally mildly nodular, no dominant mass.
Thermography	L. Suspicious 2^{0} and more vascular. Quite different from May 1969
Senography	Dense fibrocystic disease

For recall in six months in view of thermogram

November 1970 Consulted family doctor because of small nodule in right breast and referred to a surgeon.

His report is as follows:

Hard tumour in right breast at junction of upper outer quadrant and axillary tail. It is free of skin and deep fascia. There is one palpable node on medial wall of the axilla.

Treatment: Extended simple right mastectomy

Histology: Adenocarcinoma. No involvement of lymph nodes.

The senogram of June 1970 has been reviewed and even with hind sight, I would not change the report. As to the thermogram, I wonder if she may have another lesion in the left breast. Unfortunately, it will not be known if this was a false negative thermogram and X-ray report, or if this was a very rapidly growing tumour. There is a possibility that the site of the tumour was inadequately viewed on X-ray; also

there was little or no contrast in the dense fibrocystic breast.

During Phase III, the pick up rate in a highly selected group of 1017 Well Women examined clinically, by thermography and senography, was 21.6 women with breast cancer per 1000 Well Women examined. As five women had simultaneously bilateral cancers, this is a pick up rate of 26.5 tumours per 1000 Well Women examined. (There were also two asymptomatic cancers found in two women with clinical cancer in the other breast; ref. Table 20, Cases Nos. 33 and 34.)

Of the 1017 senograms done, there was a false positive rate of 1.8%.

There was a false negative rate of 0.1% (after a follow up period of between eleven and seventeen months).

All the asymptomatic cancers found by thermography and/or senography were limited to the breast.

Of the thirty-eight asymptomatic cancers in Phase II and Phase III, eight were lobular in situ cancer.

These thirty-eight cancers occurred in thirty women; six women had simultaneous bilateral lesions. The other two were subsequently contralateral as follows:-

Mrs. J. B. (Table 10, Case No. 9) presented as a Well Woman who had had a radical mastectomy two years previously and was found to have a contralateral asymptomatic lesion.

Mrs. J.W. (Table 10, Case No. 15 and Table 23) had a left mastectomy in October 1969 during Phase II. A contralateral lesion was suspected on thermography and senography in June 1970. By January 1971, the microcalcification had increased on senography and biopsy confirmed an intraduct carcinoma.

Nipple Discharge

Seventeen Well Women were found to have nipple discharge, bilateral in six cases. None of them was taking drugs of the Phenothiazine group. The results of cytological examination of this discharge are shown in Table 21.

TABLE 21

Nipple Discharge examined cytologically

Cytology Reports	23
Debris only	5
No abnormal cells	12
Histocytes and clumps of cells suggesting duct papilloma	4
Cancer cells	2

Table 22 correlates clinical findings, thermographic and mammographic findings and histology when appropriate, with the cytology. There is no constant relationship.

From work with women with clinical breast cancer, I am well aware that only a positive cytology report on a nipple discharge is significant. The finding of cancer cells is very helpful, but their absence is of no diagnostic value. This opinion has also been expressed by Gros (110) who found that in women with breast cancer and a nipple discharge, only sixty percent of the discharges showed cancer cells. The reason for this is that the involved duct may be blocked distal to the neoplasm, so that shed cancer cells do not reach the nipple in a discharge.

A positive report, however, can be most helpful as illustrated by the following case history:-

Case history of Mrs. G.C. aged fifty six.

Married at thirty four years, one child aged eighteen, born 4 years later.

15.5.69

Clinical examination:		Breasts of moderate size, generally knotty, but no dominant mass. No evidence of nipple discharge.
Thermography	Left	abnormal with 4^{o} differential.
Mammography	Left	area of punctate calcification indicating intra-duct carcinoma

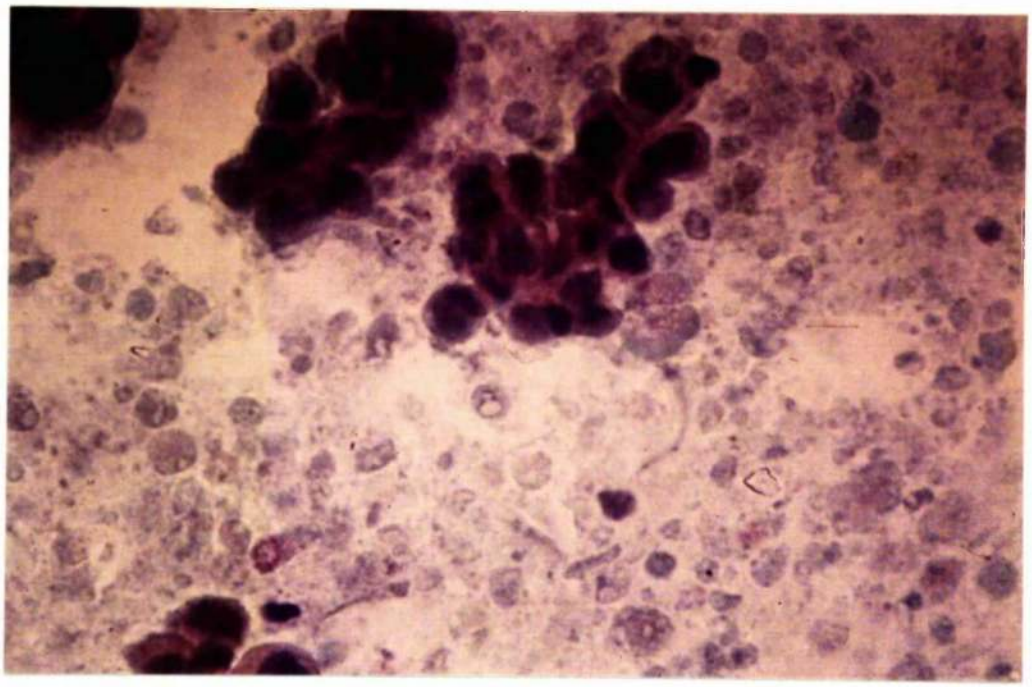
The patient, a radiographer, wife of a doctor, requested that a mastectomy be done in the first instance, rather than a biopsy.

9.6.69

When skin preparation was being done in theatre, a discharge occurred from the left nipple. A specimen was taken for examination and revealed many cancer cells.

This case occurred before we had acquired the senograph and so the mastectomy specimen was not X-rayed. It was the knowledge of the cytology report which gave grounds for insisting that further sections be cut when the pathologist issued a negative report. The final report showed an intra-ductal carcinoma.

Plate XV.



Smear of nipple discharge (Mrs.G.C.), showing many malignant cells.

TABLE 22

Correlation of cytology, clinical, thermographic and mammographic findings - with histology when applicable

	Cytology	Clinical	Thermogram	Mammogram	Histology
1.	L. Cancer cells	Generally knotty	L. Highly suspicious 4^{o}	L. Punctate calcification	Intra-duct carcinoma
2.	L. Cancer cells	Normal	L. 2^{o}	L. Punctate calcification	Refused + biopsy
3.	May, 70 Bilateral debris only	Knotty	Negative	Fibrocystic disease	-
4.	June, 70 L. debris only	Ropey areolar area	Negative	Duct ectasia	-
5.	May, 70 Bilateral debris only	Normal	Each areola warm	Duct ectasia	
	Jan. 71 I.S.Q.	Normal	L. areola 2^{o}	L. vaguely suspicious Review 3/12	-
6.	July, 70 L. Neg.	Normal	Negative	Fibrocystic disease	-
7.	Oct. 69 R. Neg.	R. Mass	R. Vasc. ++	Cancer	Chronic abscess
8.	July, 69 R. Neg.	Normal	Negative	Normal	-
9.	Dec. 69 R. Neg.	Knotty	Negative	Duct ectasia	-

10.	May, 70 L. Neg.	Normal	Negative	Fibrocystic disease	-
11.	Jan. 70 L. Blood stained No abnormal cells	Nodule L.	Very vasc. but no differential	Normal	Intra-duct papilloma
12.	Sept. 69 Bilateral negative	Normal	Negative	Normal	-
13.	June, 70 Bilateral negative	Generally knotty	Negative	Fibrocystic disease	-
14.	July, 70 Bilateral negative	Normal	L. areola 1^{o}	Normal	-
15.	March, 70 L. suggestive of duct papilloma	Normal	Mottled but negative	L. Dilated duct with irregularity of outline Senogram: Dilated duct No filling defect	-
16.	Feb. 70 Bilateral: Suggestive of duct papilloma	Normal	Each areola area hot; L.U.D 1^{o}	Normal	R. Intra-duct papilloma L. Multiple papillomata
17,	July, 70 L. Suggestive of duct papilloma	Normal	L. areola 2^{o}	Duct ectasia especially L.	
	Oct. 70 No discharge	Normal	No change	No change	-

All these women are being followed up carefully - with the exception of Case No. 2, who refuses to attend.+

+June, 1971 This patient requested biopsy. To date, the histology has revealed only a group of malignant cells in a blood vessel. Further sections are being prepared. As the specimen weighs 5-lbs. 10-ozs. this will be a time consuming procedure.

TABLE 23.

Phase 111:- Follow-up of Doubtful Senograms.

Total number of doubtful senograms.			87
Lost to follow-up		7	
Senogram, progressive lesion, but no palpable lesion- for biopsy		7	
Senogram, increase in punctate calcification	6		
Biopsy reports:			
J.W. Intraduct carcinoma (Jan.71)			
M.M. Intraduct carcinoma (Ap.71)			
J.A. Intraduct carcinoma (Mar.71)			
D.B. Intraduct carcinoma (Mar.71)			
J.A. Papillomatosis (Mar.71)			
J.H. Papillomatosis (Feb.71)			
Senogram, increase in doubtful opacity	1		
Biopsy report:			
J.B. Cystic disease (Ap.71)			
Senogram, (doubtful calcification), calcification now obviously benign		11	
Calcification unchanged		10	
Senogram, (vague opacity), now considered to be normal		11	
-now considered fibrocystic disease		5	
Senogram, (asymmetrical duct pattern), no change		9	
Senogram, (unilateral increased vascularity), -unchanged		9	
-now considered normal		8	
-now considered fibrocystic disease		10	

One patient, with a suspicious thermogram, but negative clinical examination and senogram in June, 1970, was recalled in January, 1971. On this occasion, the senogram revealed a vague opacity with highly suspicious calcification. Biopsy has been carried out and the histology showed a very minute focus of carcinoma.

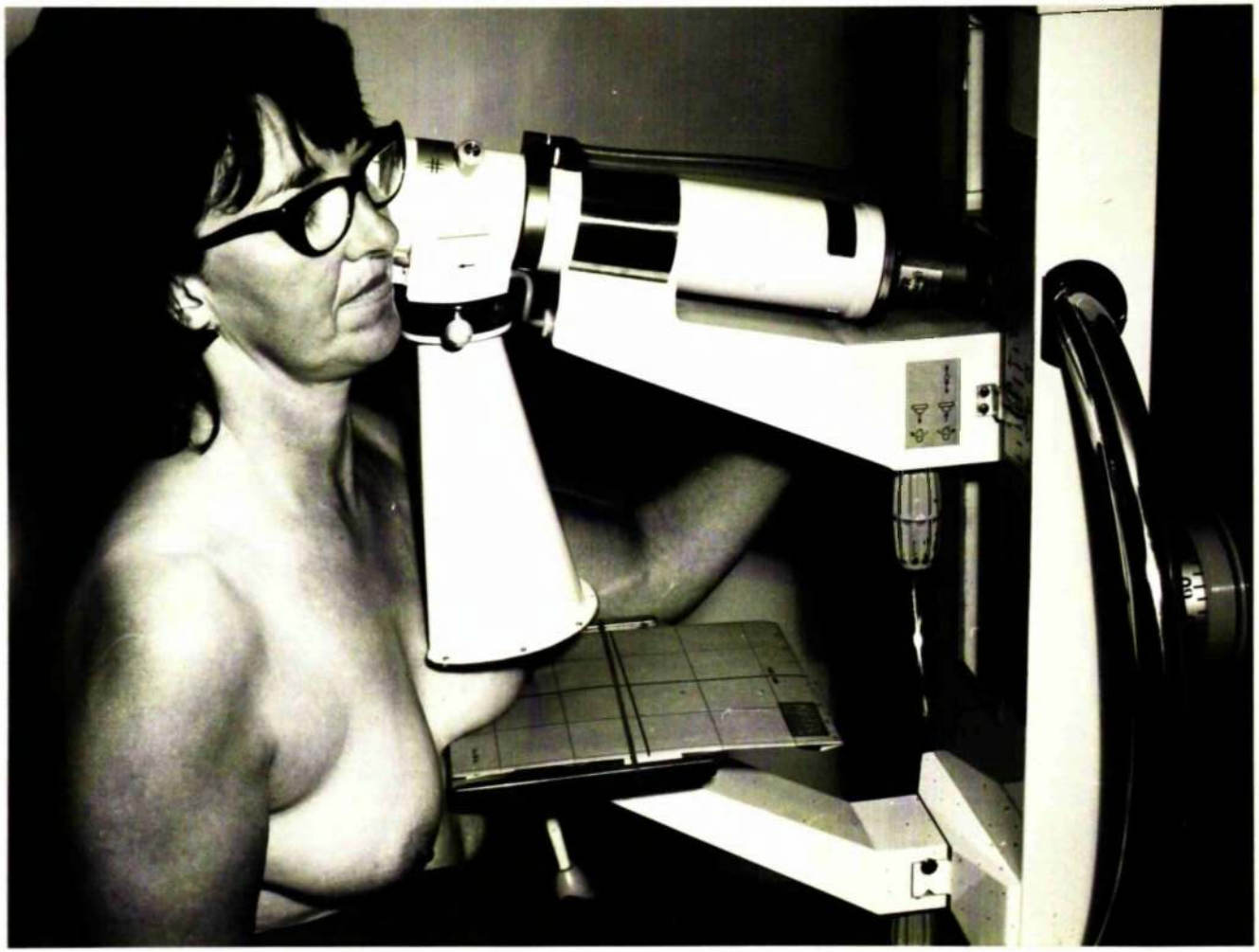
During 1971, an attempt has been made to carry out the annual review of those women, last reviewed during the corresponding months of 1970. Appointments are on average six weeks over the year as a result of the cumulative effect of a local bus strike, the national electricity strike (when there was a voltage drop of such degree that the senograph and thermovision were affected) and the postal strike.

Three patients, all considered within normal limits on clinical examination, thermography and senography during April, 1970, now await biopsy. When seen for routine annual review in late May, early June, 1971, they have no palpable lesions but abnormal thermograms and highly suspicious punctate calcification on senogram. Six hundred and one have been passed as within normal limits at the second annual screening.

There follows a series of representative mammograms It should be noted that the details of mammograms do not reproduce well, in prints, especially microcalcification found when screening the films with a hand lens.

POSITIONS FOR SENOGRAPHY.

Plate XV1.



Position for a supra-inferior view. The photograph has been taken before compression was applied by lowering the cone.

Plate XV11.

This plate and plate XV11b. show the position for a lateral view, as demonstrated in the Senograph brochure. I have found that a much more extensive projection of the axillary tail is obtained when the shoulder is relaxed and the arm hugs the cone, as in plates XV111 and XV111b.

Plate XV11b.

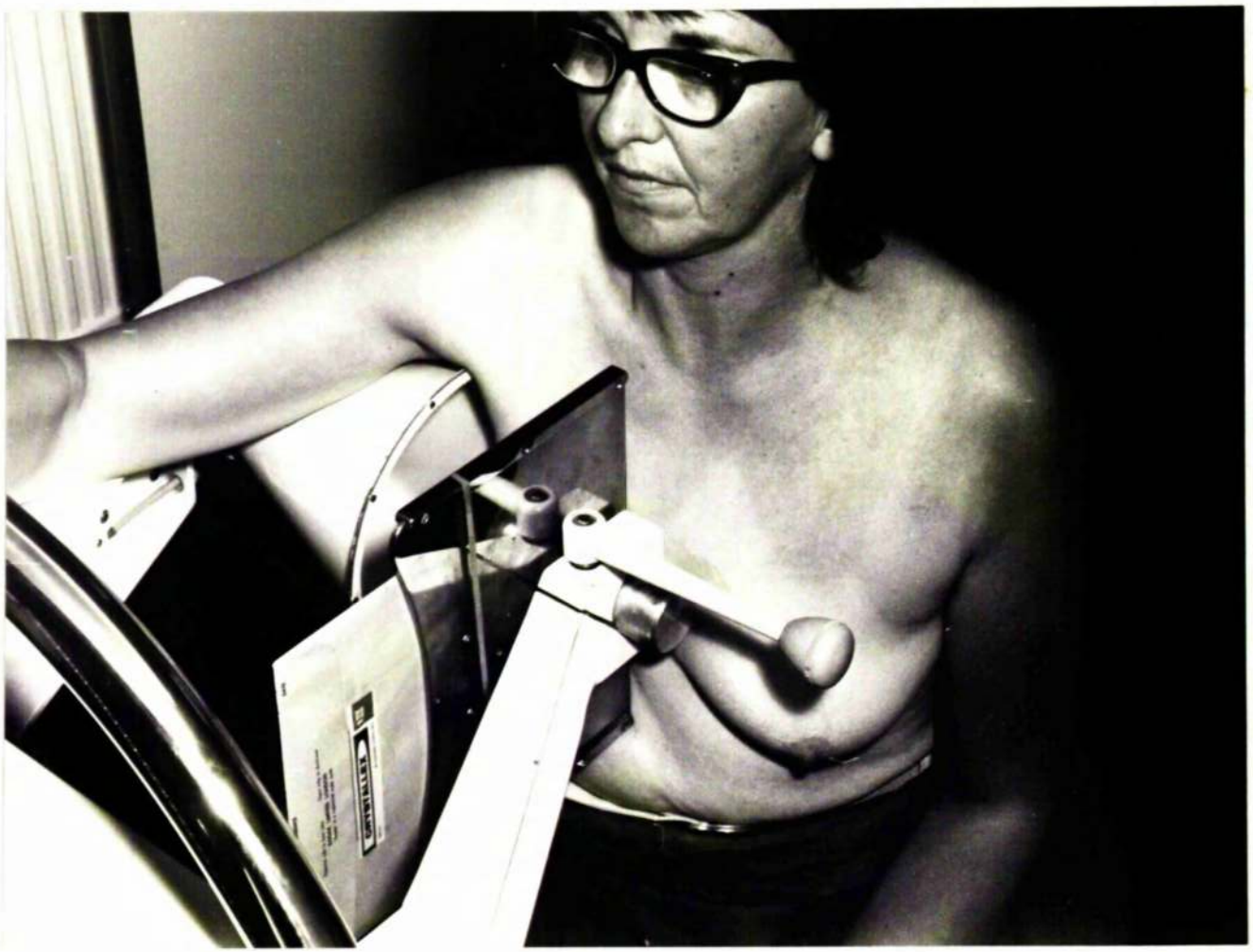


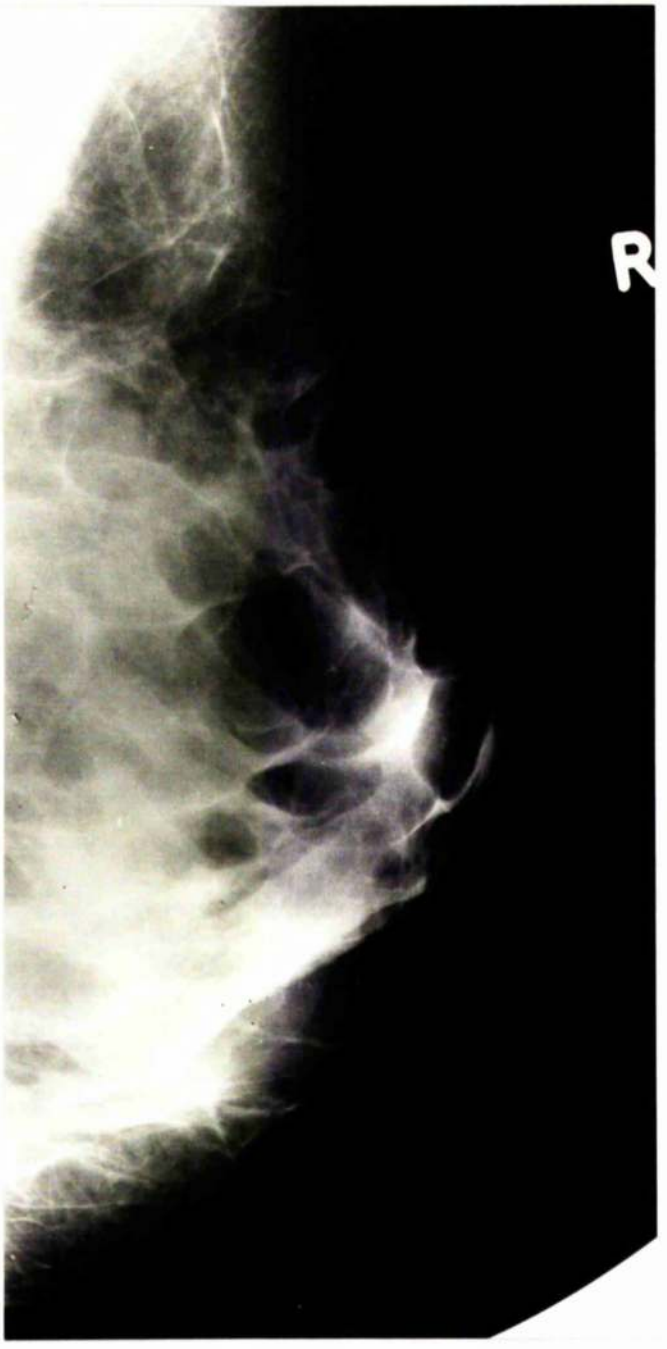
Plate XV111.

Plate XVIIIb.

Plate XIX.

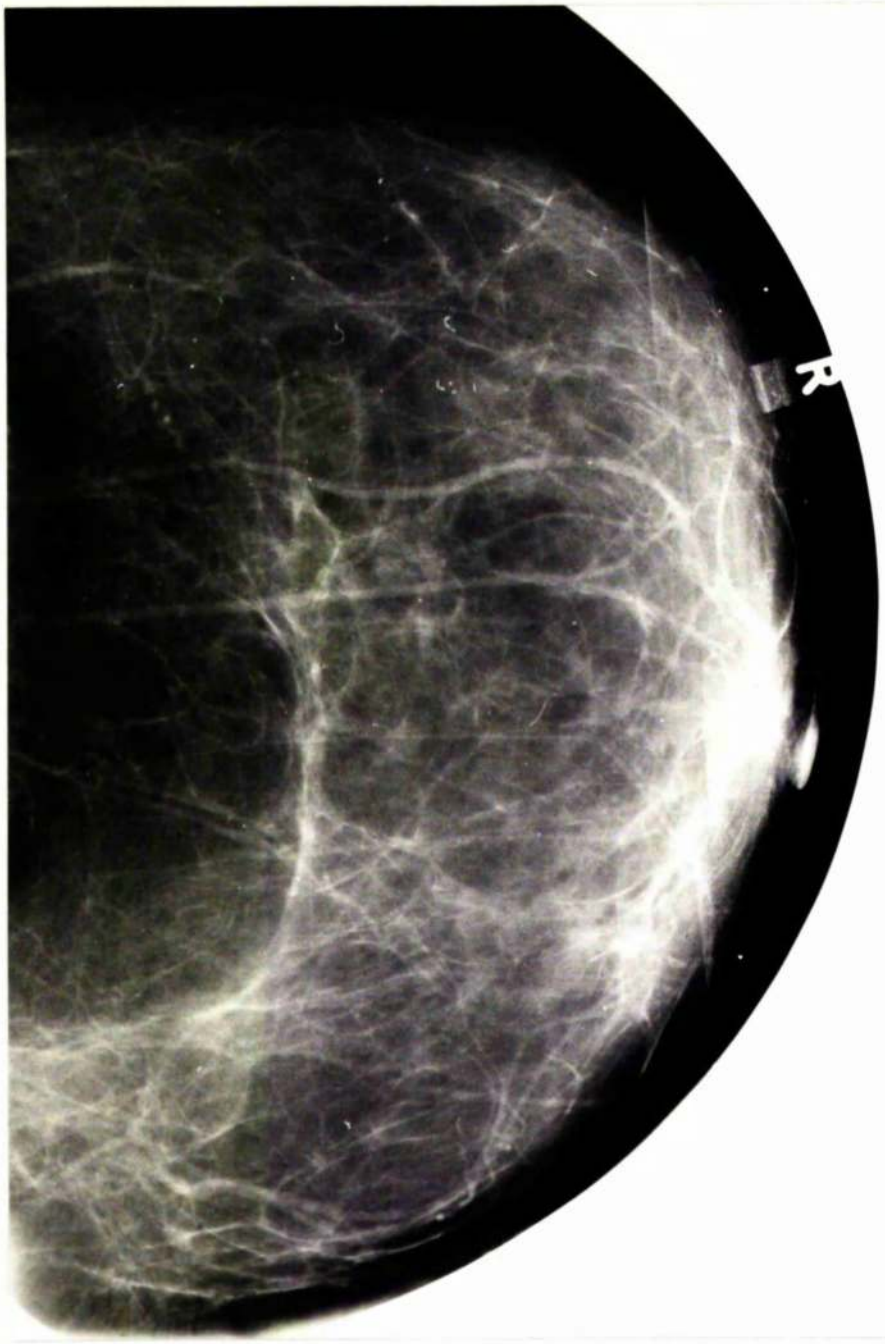
Position for axillary tail view. The tube and base plate are at an angle of 30 degrees. This view is not taken routinely, being reserved fer very small breasts in which the two standard views are judged to be inadequate.

Plate XX.



Normal senogram, patient aged 39 years.

Plate XXl.



Normal senogram, patient aged 61 years. This shows the replacement of glandular tissue by fat with increased prominence of the trabeculae. This gives good contrast for a malignant opacity.

OPACITIES.

Plate XXll.

Opacity - benign. This plate shows a well defined opacity due to a fibroadenoma. Patient aged 36 years.

Plate XXlll.

Opacity- benign. This plate shows the well defined opacities of multiple cysts. Patient aged 41 years.

Plate XXlV.

This is a senogram of the same breast as plate XXlll. It was taken immediately following aspiration of the cysts which were then inflated with an equal volume of air. Note the clear, well defined inner cyst walls with no evidence of an intra-cystic lesion. The cytology report on the aspirated fluid was negative.

Plate XXV.

This is a senogram of the same breast as plates XXlll and XXlV, taken six months after aspiration of the cysts. There has been no recurrence.

Plate XXVI.

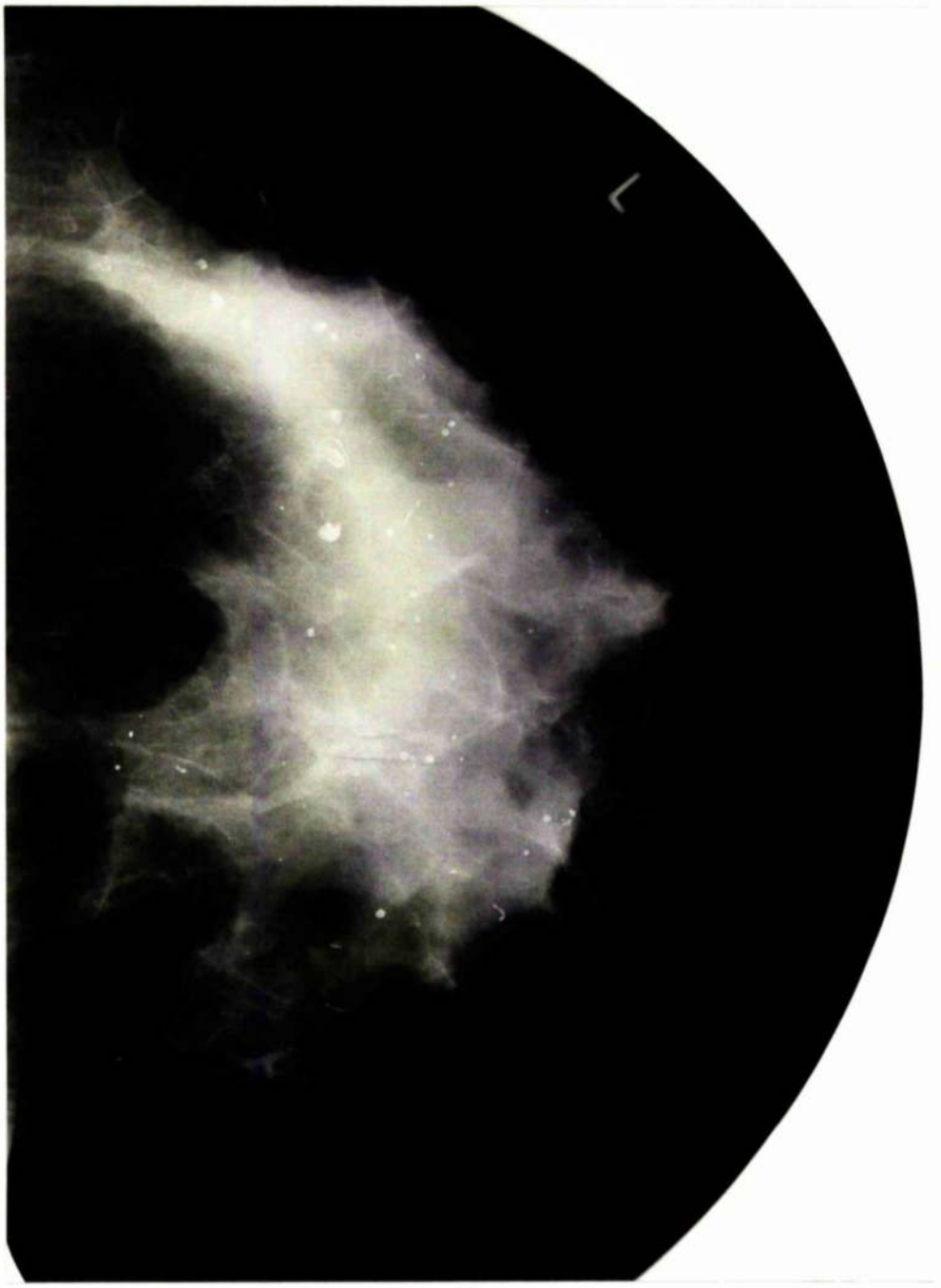
Opacity- malignant, patient aged 57 years. This cancer, with spiculated outline,in a very large,fat and pendulous breast was not palpable. The senogram demonstrates fine calcification in the tumour (not seen in the print);also greatly increased vascularity compared to the contra lateral breast.

Plate XXVll.

This is aslice of the mastectomy specimen of the breast shown in plate XXVl, and depicts opacities which are lymph nodes. Before stating "the nodes are not involved", it is essential to ensure that all the removed nodes are examined histologically. For this purpose, the specimen is sliced and X-rayed; then, guided by the film, the nodes are dissected and the specimen re-Xrayed. It is possible for a large node to superimpose a small node which is revealed on X-raying the remaining specimen.

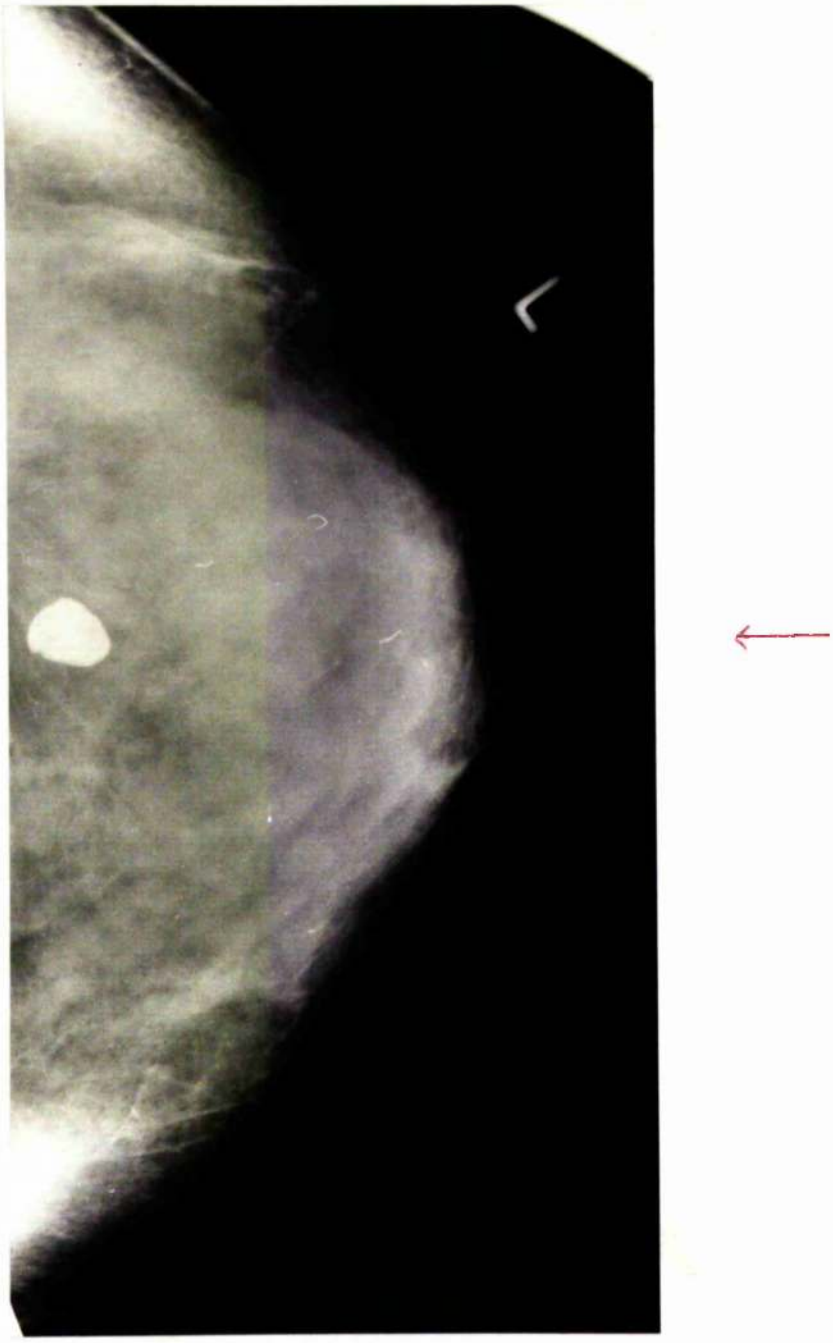
CALCIFICATION in the BREAST.

Plate XXVlll.



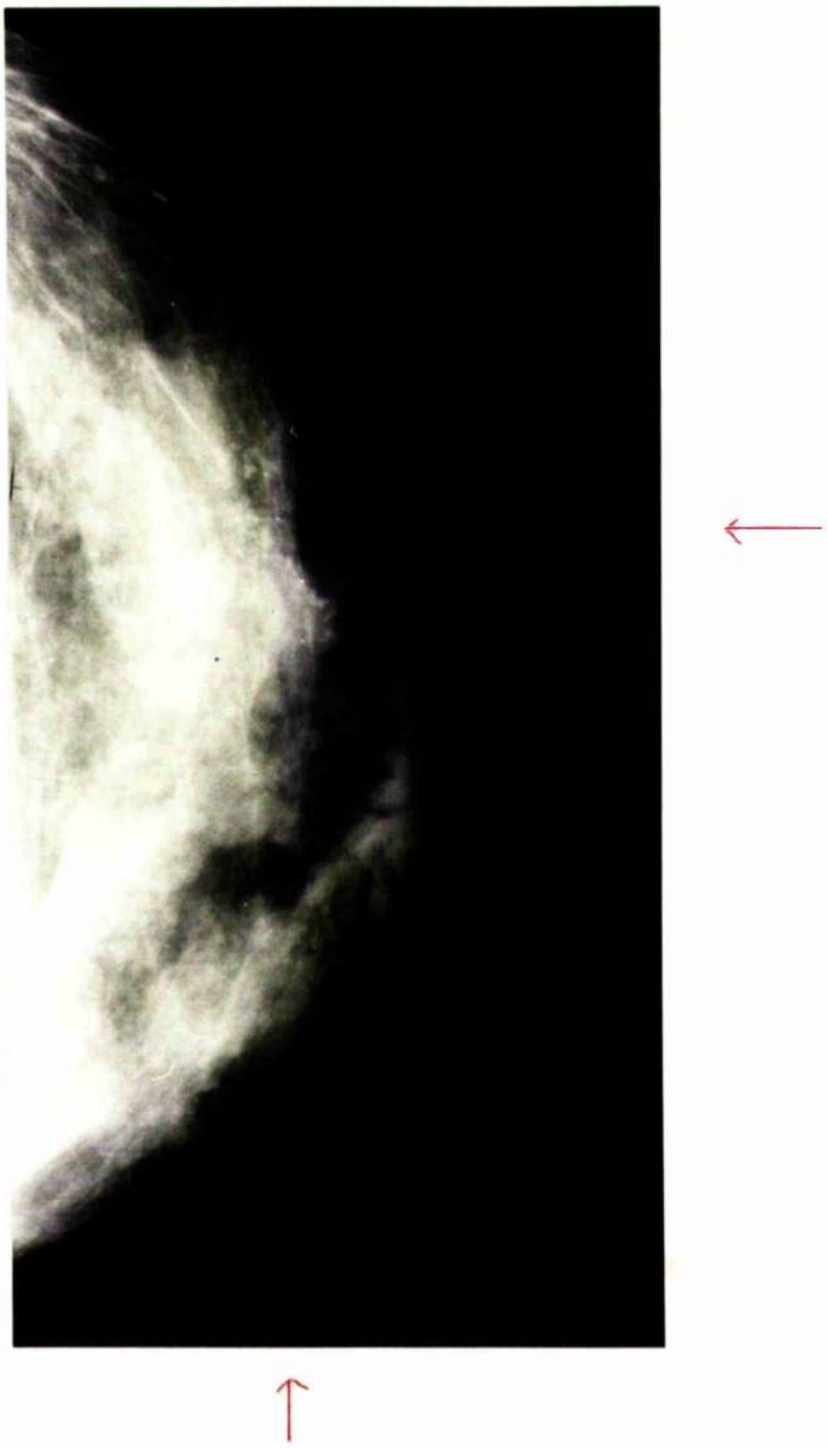
This calcification is benign. It is gross, well scattered and due to old secretory disease in a woman, aged 61 years.

Plate XXIX.



This is gross calcification in a fibroadenoma, in a woman of 58 years.

Plate XXX.

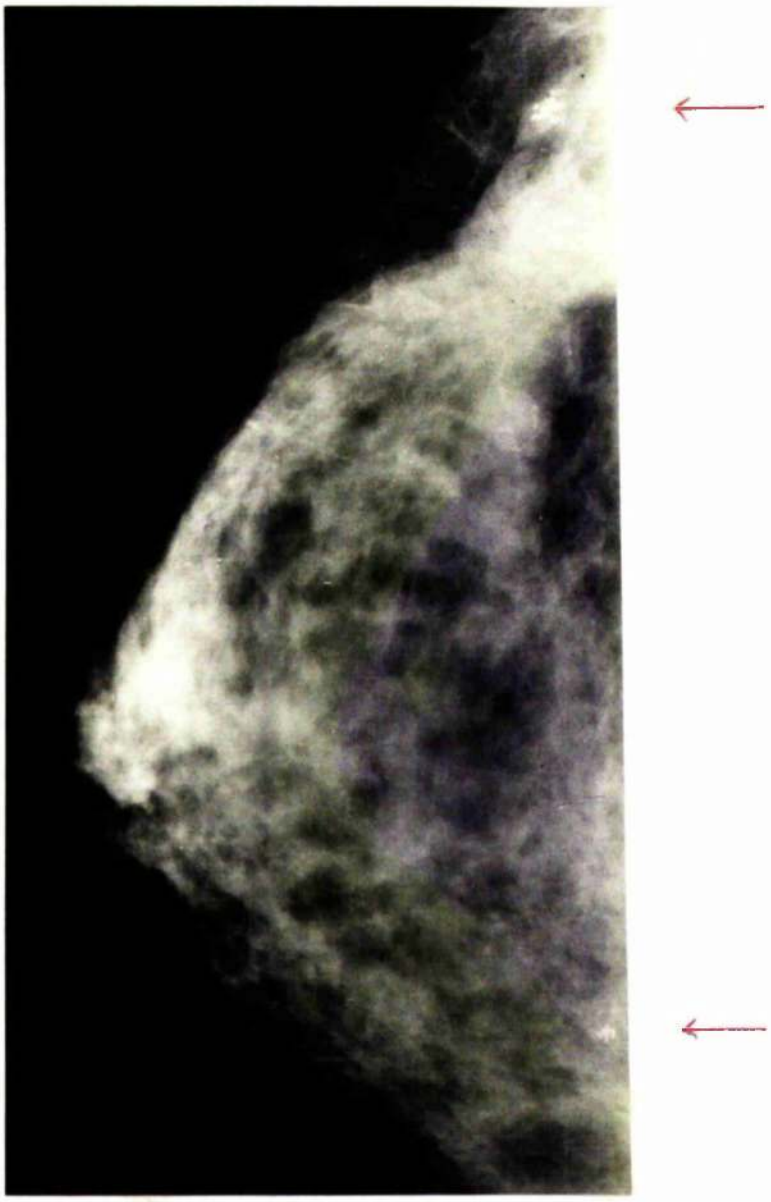


This calcification is fine, bizarre and localised. The diagnosis of intraduct carcinoma was confirmed histologically.

Plate XXXl.

This is the sliced specimen of the breast in plate XXX. The microcalcification in slices one and two was the site of the lesion.

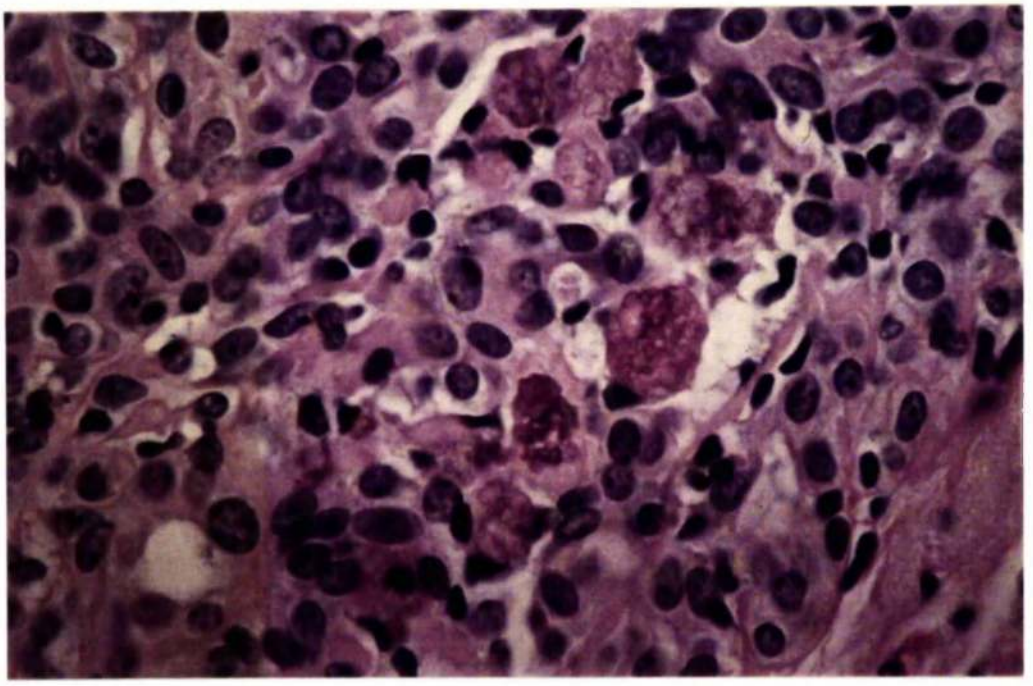
Plate XXXll.



This shows two foci of microcalcifications. The diagnosis of multifocal intraduct carcinoma was confirmed histologically.

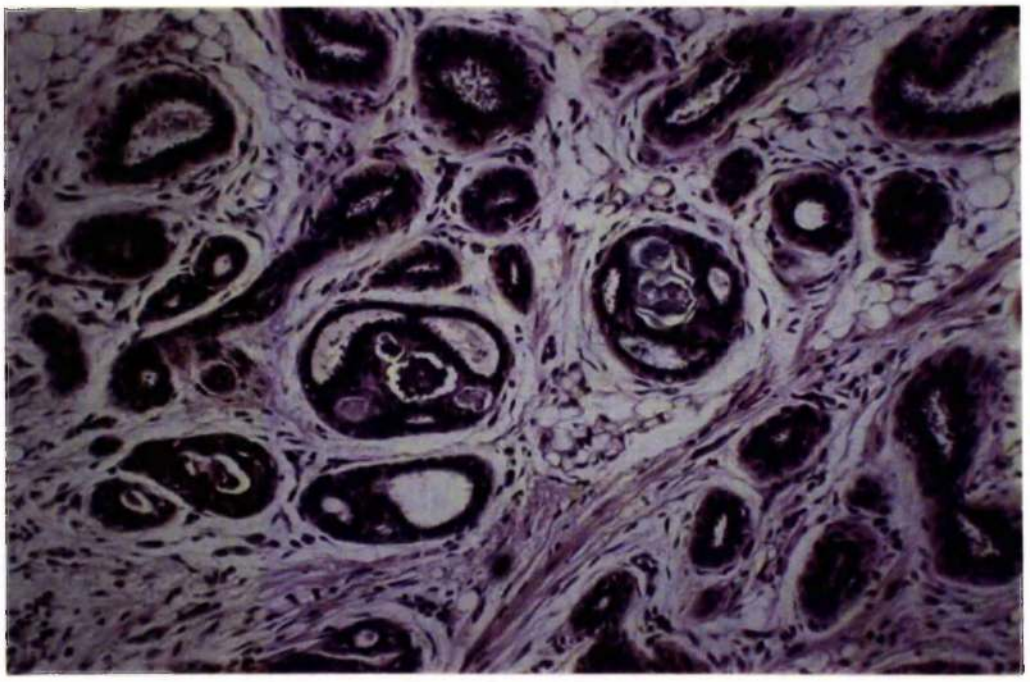
Histology of breast shown in plates XXX and XXXl.

Plate XXXlll.



Area of intraduct carcinoma, showing microcalcification.

Plate XXXlV.



Adjacent area of marked epitheliosis with calcification in two ducts in centre of the field.

DIAGNOSTIC DIFFICULTIES.

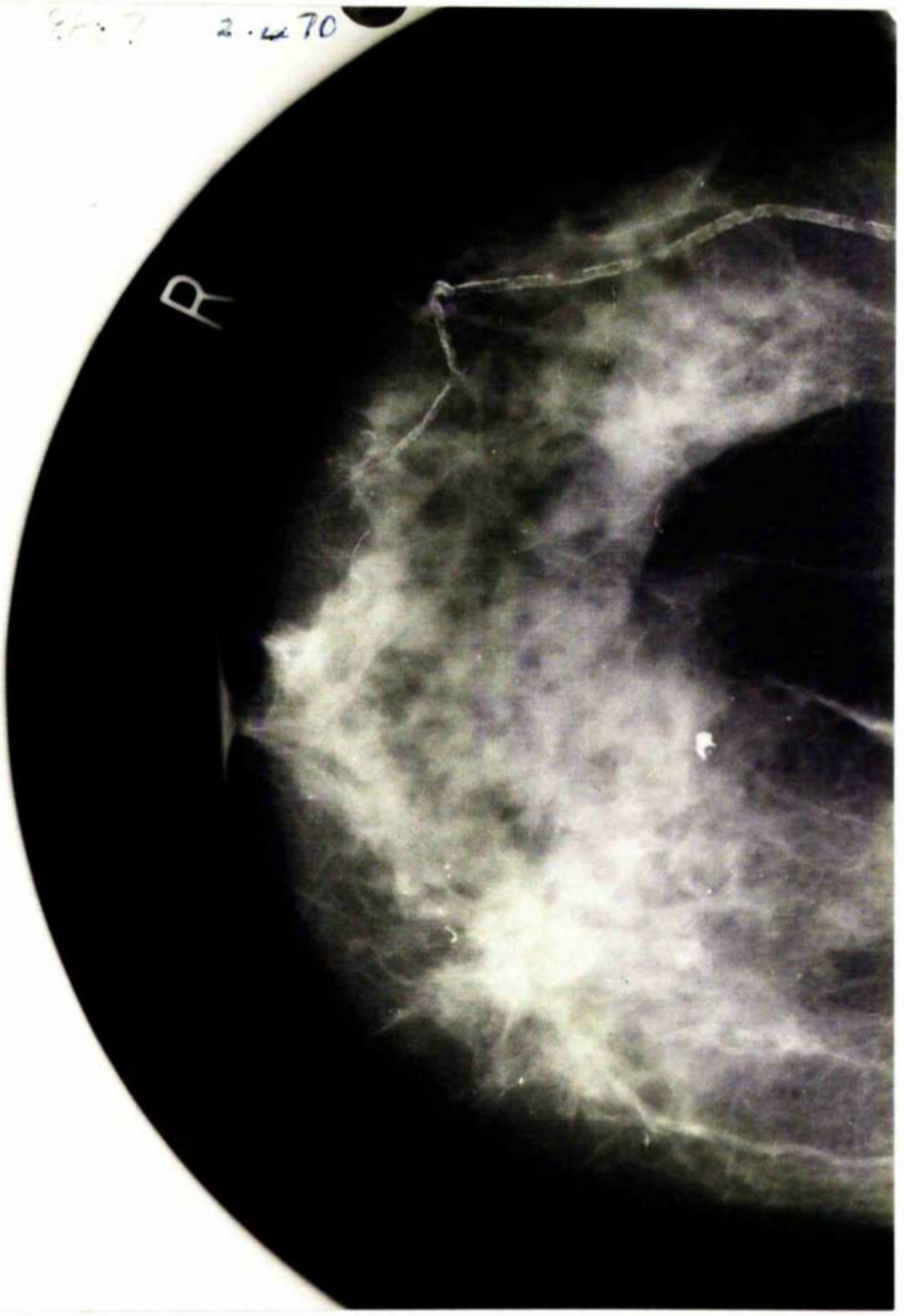
Plate XXXV.

Adenosis with its multiple small opacities which may mimic or obscure a malignant lesion. Comparison of supra-inferior and lateral views and serial films at three to four months interval is helpful in these circumstances. This 45 year old woman remains negative on clinical and thermographic examination and with a similar senogram after fifteen months.

Plate XXXVl.

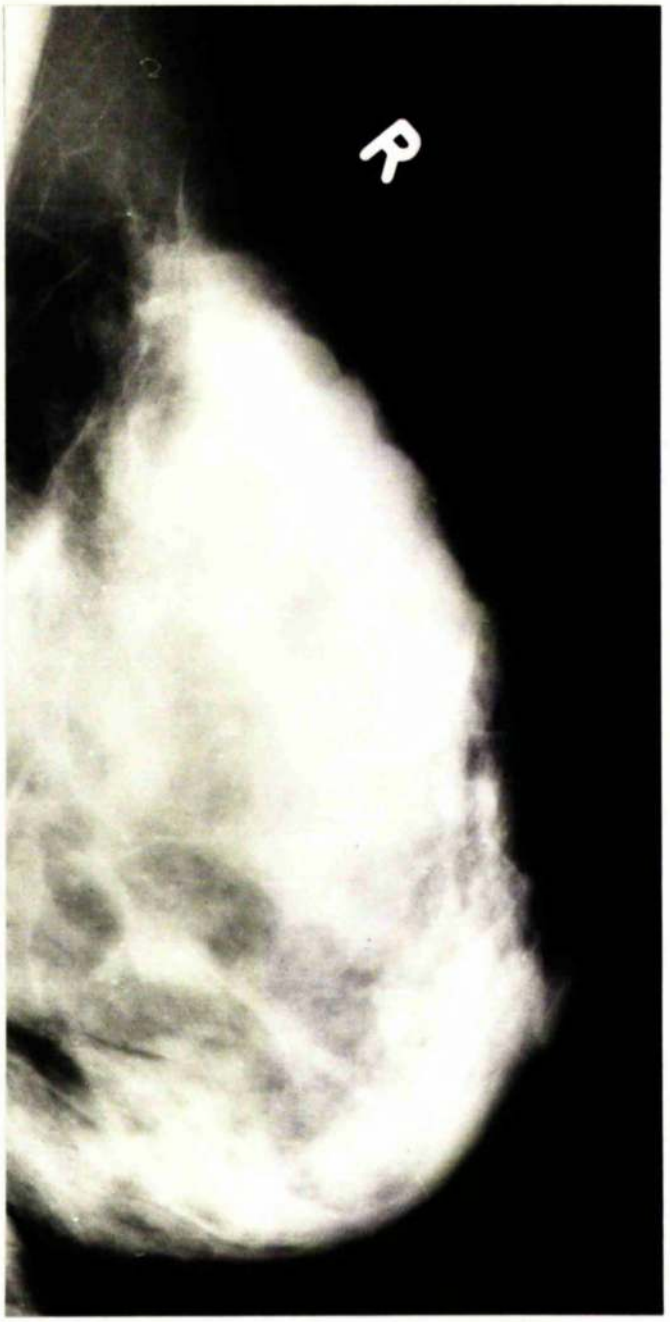
This shows the uniformly dense senogram of a 34 year old woman with very nodular breasts. It is impossible to give any opinion on such a senogram.

Plate XXXVll.



This senogram of a 56 year old woman shows the irregular opacities of sclerosing adenosis, tortuous thickened ducts and gross calcification as "pearls"; vascular calcification is also present. Such a picture could obscure a small cancer and, of course, this type of breast, with a wide spectrum of dysplasia, is a high risk. Again, comparison of films is helpful.
Clinical and thermographic examinations are within normal limits and a repeat senogram, after six months, is unchanged.

Plate XXXVlll.



This is a worrying case of a 37 year old woman whose senogram shows considerable fine calcification in both breasts, mainly in the upper outer quadrants. Much of it is obviously benign, but there are several localised groups of punctate calcification of doubtful significance. She has been observed over a year now without any change. It is unusual to find so much calcification in this age group.

Case history, illustrative of routine

Mrs. E.P.
(No. 23 in TABLE 20)
Aged 50 years, married at 22 years but no family.

Five years post-menopausal.

22.10.69

Clinical examination; moderate sized breasts, normal.

Thermography: Highly vascular pattern, right 1^{o} warmer than left.

Mammography: Bilateral minimal calcification

Opinion: Repeat in three months

17.12.69

Clinical examination; no change

Thermography: Highly vascular pattern with 3^{o} differential on right, but not isolated hot spot.

Senography: Right:- Minimal micro-calcification in upper outer quadrant.
Left:- Group of calcifications suggesting intraduct carcinoma.

Opinion: Bilateral biopsy advised

(This was the first patient for whom the Senograph was used in this survey).

19.12.69

Bilateral biopsies carried out.

X-ray of the specimens was performed.

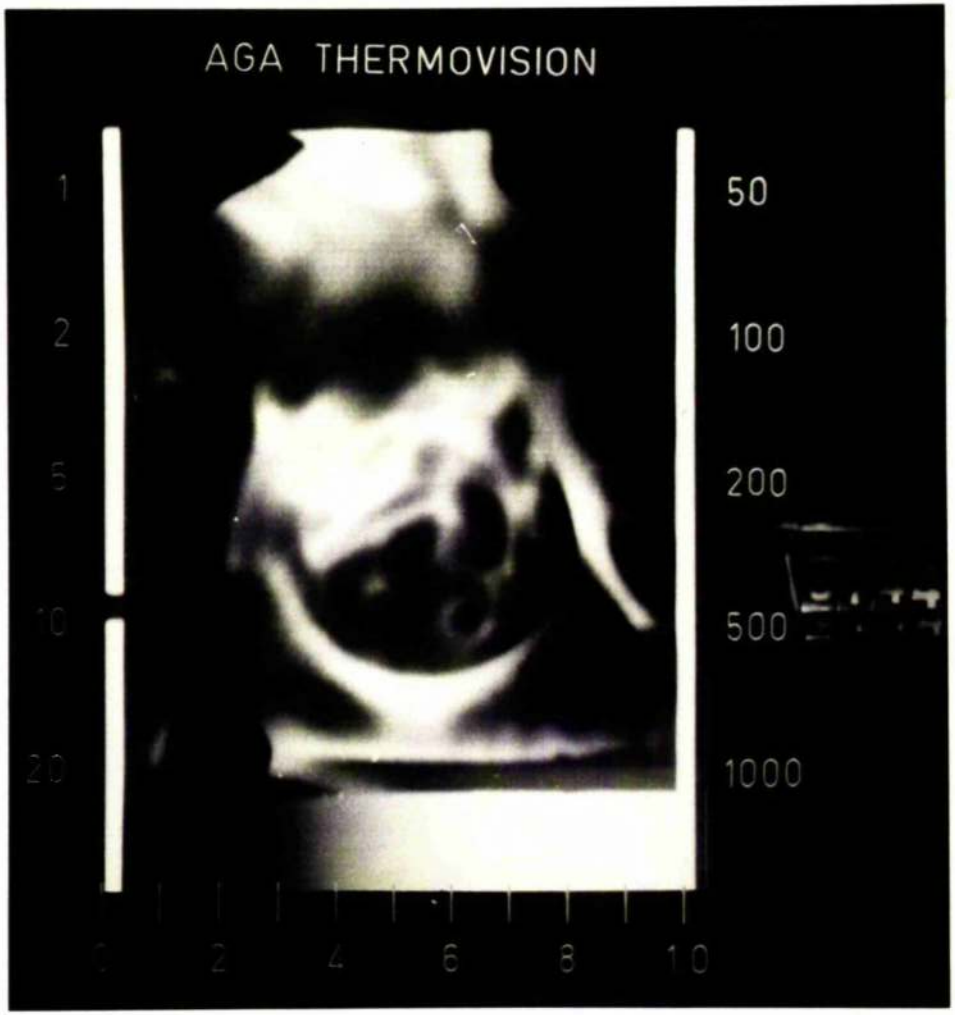
Histology: Right: Lobular carcinoma in situ.
Left: Intra-duct carcinoma

Immediately after Christmas, right simple and left modified radical mastectomies were performed.

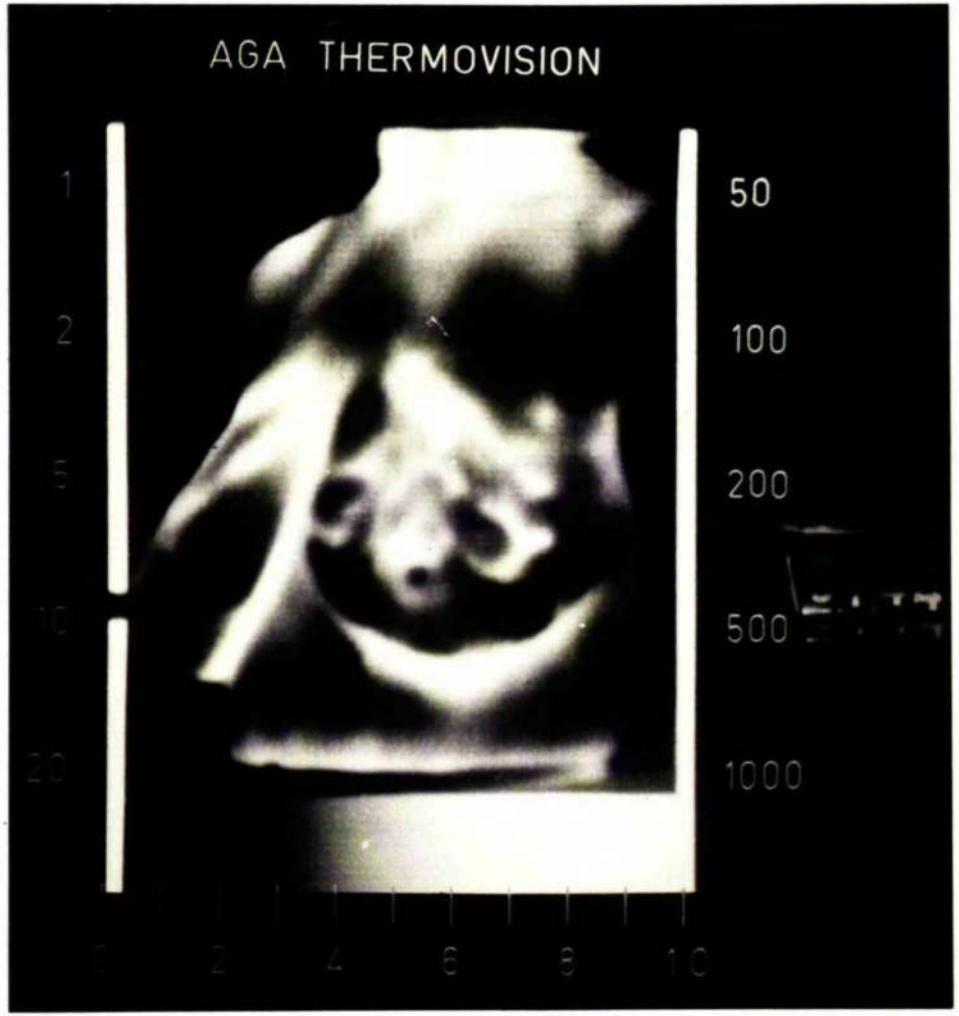
Mrs. E.P. was last seen by me on 12.3.71; she is very fit.

Plate XXXV111. Mrs.E.P.

Right oblique.



Left oblique.



Thermogram showing a highly vascular pattern.

Plate XL. Mrs.E.P.

Senogram of Mrs.E.P.'s left breast, showing a group of microcalcifications indicative of an intraduct carcinoma. The senogram of the right breast (not shown) had a more diffuse area of microcalcification in the upper outer quadrant.

Plate XLl. Mrs.E.P.

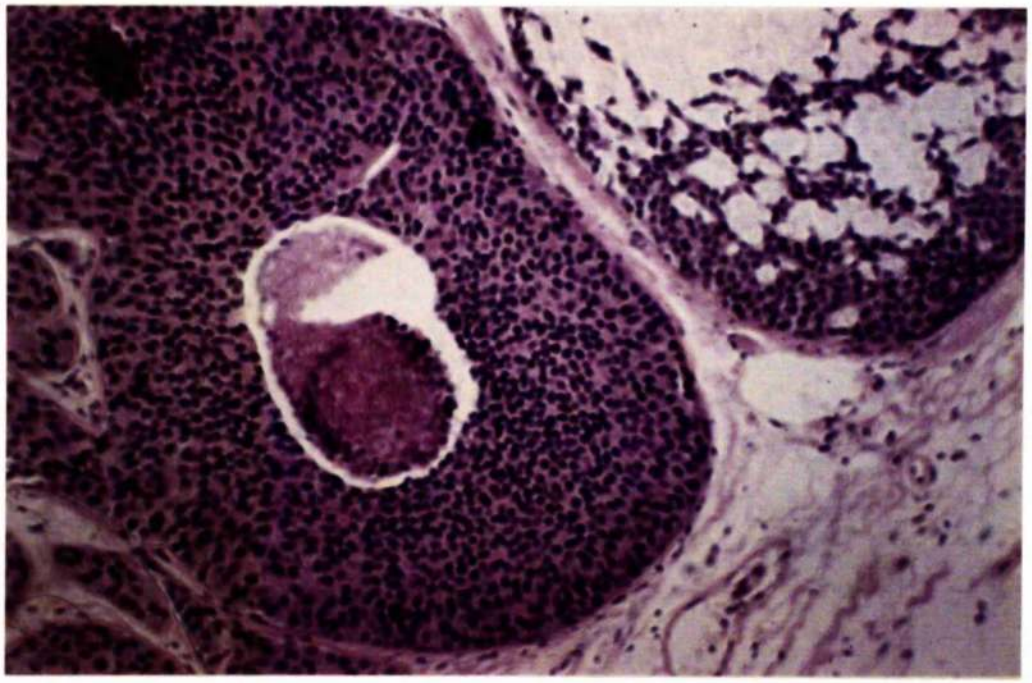
The biopsy of the left breast, showing a 0.5cm cancer.

Plate XLll. Mrs.E.P.

X-ray of biopsy specimen, left breast.

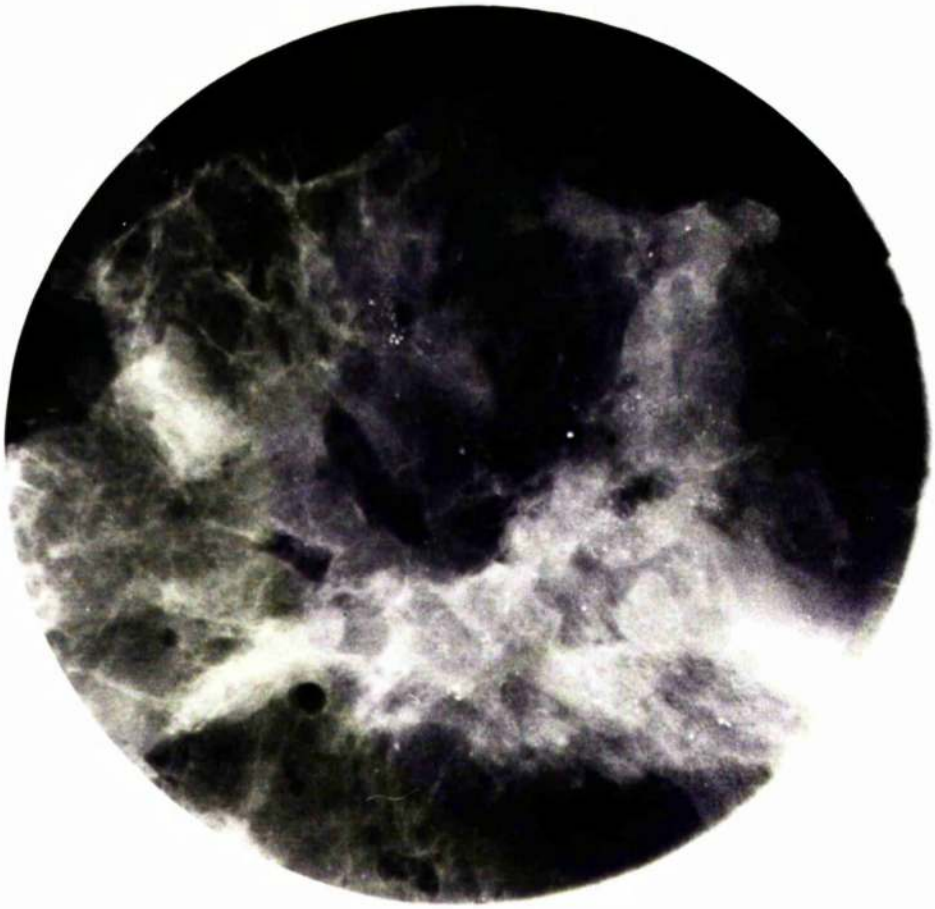
Calcification was the site of tumour.

Plate XLlll. Mrs.E.P.



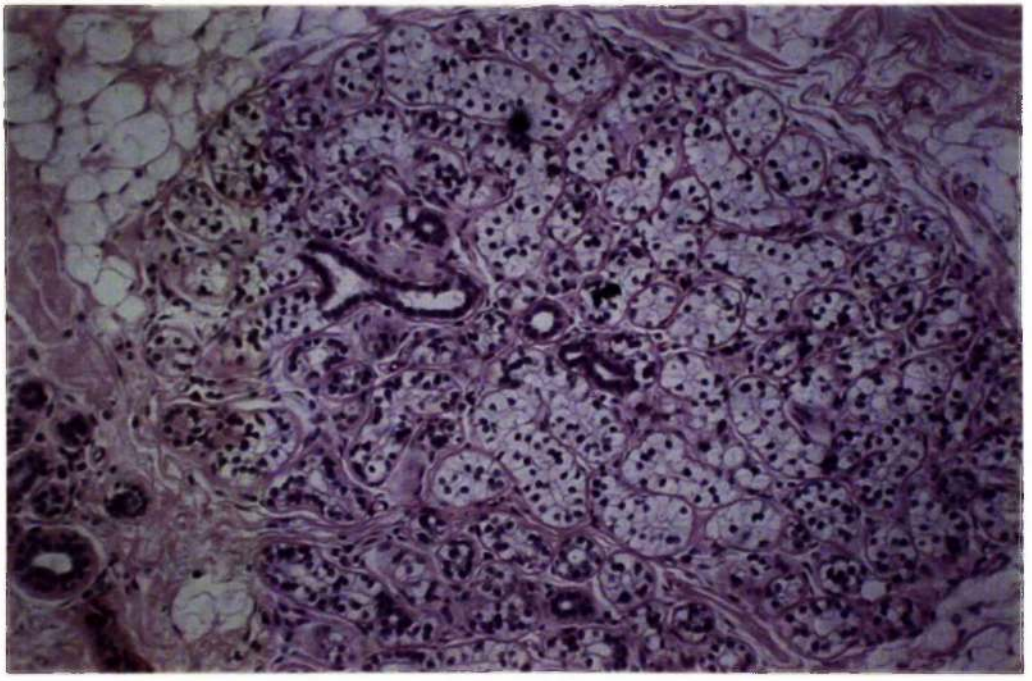
Histology of left breast - intraduct carcinoma with calcification.

Plate XLIV. Mrs.E.P.



X-ray of biopsy specimen, right breast, showing fine bizarre calcification.

Plate XLV. Mrs.E.P.



Histology of right breast - lobular carcinoma in situ.
Note that there is no calcification in the affected lobule.
In such lesions, the calcification occurs in the adjacent areas rather than in the malignant lobule.

DISCUSSION

Much is heard these days about the "dreadful toll of the roads". There is little public concern, however, about the wastage of life due to breast cancer, yet TABLE 24 shows an interesting comparison of death rates.

TABLE 24

Extracts from Registrar General's Reports			
	1968	1969	1970 (first and second quarter)
Road Fatalities (males & females)	6,250	6,558	3,873
Breast cancer (females only)	10,204	10,622	5,480

Until a way of preventing breast cancer is found or a radical change in the method of treatment is developed, early diagnosis would appear to offer the greatest hope of improving the survival of breast cancer patients.

In this thesis, an attempt is made to evaluate various methods of early diagnosis.

Clinical examination alone, as in Phase I, was relatively unproductive. As has been said (pp. 1) in 65% of patients the cancer has spread beyond the breast by the time it becomes palpable.

Clinical examination with thermography (Phase II) as an initial method of screening offers greater hope of picking up the pre-clinical lesion.

The accuracy of thermography in clinical cancer has been well documented as in TABLE 25.

TABLE 25

Percentage of clinical cancers giving positive thermographic findings

Gros (110)	90%
Wallace & Dodd (116)	87%
Aarts (115)	72%
Lloyd Williams (38)	94%
Ross (9)	85%
Forrest (117)	44.4%
Nathan (118)	68%
Stark (*)	80%

* Series of clinical breast cancers, not in this Well Women review. The twenty percent which were thermographically negative were all scirrhous cancers.

In Phase II the percentage of thermograms sufficiently suspicious to require further investigation which revealed no conclusive evidence of malignancy, is similar to that reported by other workers - TABLE 26.

TABLE 26

False "positive" thermograms

	"False Positives"
Hitchcock et al (111)	13.5%
Jones & Draper (112)	15%
Wallace & Dodd (32)	13.2%
Samuel & Young (113)	13.8%
Hoffman (114)	7.4%
Aarts (115)	28%
Phase II	10.9%
Phase III	21.9%

The greatly increased number of abnormal thermograms in Phase III was due to the increase in the percentage of women with fibrocystic dysplasia in this highly selected group.

The greatest difficulty in interpretation occurred in the 36-45 age group with highly vascular patterns (TABLE 8), although the false

negative thermograms are evenly distributed through the ages 35-63 (TABLE 11).

Because of the relatively high incidence of false positive thermograms, I have not considered an abnormal thermogram alone to be sufficient indication for biopsy, but purely as an index of suspicion to be followed up. At subsequent examination, nine of these women had clinical or senographic findings which warranted biopsy; the histological findings were as in TABLE 27.

TABLE 27

Histology of biopsies in women with "false positive" thermograms, subsequently associated with positive mammograms.

Total 9		
		Latent time in months
Carcinoma	4	6 9 14 15
Epitheliosis	1	6
Fibroadenoma	1	6
Adenosis	1	10
Papillomatosis - gross	1	16
Extreme adenosis with very active cellular element	1	6

One further patient, considered at the time to be a false positive thermogram with negative clinical examination and mammogram, developed a clinical cancer twenty-six months later, having defaulted from follow-up.

Wallace and Dodd (116) reported nineteen women, with positive thermograms but negative clinical and X-ray findings, and who developed carcinoma within three to twenty-four months. This would suggest that considerable biological activity in a very small lesion can cause an abnormal thermogram before it is apparent on X-ray. It is unusual to visualise, on X-ray, a breast lesion less than 5 mm. in size.

Recently, in an attempt to reduce the percentage of false positive thermograms, and on the advice of Professor Gros, I have been taking an additional measurement on thermography. Gros is of the opinion that a breast temperature of 1.5 degrees or more above that of the mid sternum is indicative of a malignant lesion.

Correlating this measurement with patient age, week of the menstrual cycle in pre-menopausal women, oral contraceptives, thermogram pattern and senogram, no significant relationship in equivocal thermograms has emerged as yet. In normal thermograms, of all three

patterns, 96% have given a sternal temperature equal to the highest breast temperature or higher. (The average over 356 thermograms is sternal temperature of plus 1° C.) I plan to continue this observation in a group of 1000 consecutive thermograms.

Meanwhile, it would appear that benign conditions, for example, dysplasias, can have areas of increased biological activity equal to that of malignant lesions and indistinquishable by thermography.

When considering the question of the false negative thermogram, I have come to doubt the statement of Wallace and Dodd that absolute temperatures were not important in breast thermography.

At present, those cancers which do not give a differential temperature of 1.5° C. or more are assumed to be in a state of low biological activity at the time of the examination, and certainly, the fact that scirrhous cancers are almost always cold on thermography supports this view (ref. TABLE 25).

If, however, the absolute temperature of the breasts (i.e., the breast tissue as distinct from surface skin temperature) is high, then this could mask a differential temperature over a cancer - just as a hot spot can be missed when there has been insufficient cooling

of the skin.

Recent improvements in thermography equipment make it possible now to take absolute temperature measurements. This is an aspect which must be investigated.

Among recent technical advances in thermographic equipment, is the production by Aga of a colour thermovision. Each isotherm band is represented by a colour so that the temperature range progresses through the spectrum. I am indebted to Dr. Nicholson of The Department of Medical Physics, Westminster Hospital, London, for access to a colour thermovision. After a forenoon spent with this equipment, I am of the opinion that a colour oscilloscope will not improve the accuracy of breast thermography.

For the inexperienced, however, colour make make interpretation of thermograms easier.

To date, I am unaware of any published figures for false negative thermograms in Well Women. The percentage of false negative thermograms in Phase II is 0.11%, i.e., developed a clinical cancer within twelve months (ref. TABLE 11).

The advantages of thermography are:-

1. Although the capital cost of equipment is high, the actual technique is inexpensive to perform.
2. With experience, it is a relatively simple and quick test, which can be repeated at frequent intervals.
3. There is no radiation hazard.
4. An abnormal result raises the "index of suspicion" in subsequent senography.
    (a) It is specially useful in the small glandular breasts which are difficult to X-ray; whose X-rays are difficult to interpret because of lack of contrast.
    (b) A thermogram in the lateral oblique view gives good information about the axillary tail which may not be easy to X-ray adequately in the small breast because
        (i) it is difficult to project on to film;
        (ii) it contains little fat and so there is little contrast.
5. The fact that each woman has an individual characteristic pattern is most useful in follow-up thermography.

The disadvantages of thermography are:-

1. All cancers are not hot - if of low grade activity at the time of examination. Clinical cancers of a scirrhous nature are almost always cold on thermography.

2. A small cancer in a large fatty breast may be too well insulated to give a "hot spot" but the fat breast is ideal for X-ray.
3. If there are bilateral cancers, they may give bilateral signs with resultant lack of differential, and could therefore be considered as negative. In four women with bilateral asymptomatic cancer, the thermograms were so vascular that this of itself raised my suspicions.
4. All thermographic signs of cancer can occur in benign conditions.
5. Occasional anatomical aberrations can cause false positives.
6. As yet, the available equipment is not ideal.

Nevertheless, many authorities, Samuel (119), Lawson (34), Connell (120), Isard (121), Swearingen (122), Wallace and Dodd (116), and Melander (123) consider that thermography is a worthwhile initial method of screening Well Women, and certainly the pick up rate in my series would confirm this. Using clinical examination with thermography as an initial screening, withmammography in those with abnormal findings, there was a detection rate for early breast cancer of 2.44 per thousand (3.4. per thousand in age group over 35 years). This compares favourably with pick up rates by other workers in this field - as shown in TABLE 28.

TABLE 28

Pick up rate of cancer in Well Women by clinical examination and thermography.

	Rate per thousand
Hoffman (114)	2.07
Hitchcock (111)	0.4
Stark	2.44

These figures are not strictly comparable as age groups differ.

With the knowledge that all breast cancers are not hot on thermography, it was decided to screen a number of Well Women using clinical examination, thermography and senography in each case. Gerschon-Cohen (124), Isard (121), Swearingen (122), Gros (125) have indicated that the employment of all three modalities would increase the accuracy rate to well over ninety percent.

In view of the cost of such a scheme in time and money, and our limited resources, it was decided to apply it to a high risk group only - a decision which the results fully justify.

In 1017 of these high risk women, the pick up rate was 21.6 with breast cancer per thousand Well Women examined. As five women

had simultaneously bilateral lesions, this is a pick up rate of 26.5 tumours per thousand women. After a follow up period of eleven to seventeen months, there is a false negative rate of 0.1%.

Advantages of Mammography

1. X-ray will show lesions as small as 5 mm., especially when associated with calcification which is frequent in intra-duct and scirrhous carcinomata.
2. Mammography is more accurate in differentiating benign and malignant lesions, although it is not possible to differentiate a carcinoma from epitheliosis if the only sign is calcification.
3. Better localisation is possible by X-ray.
4. The Senograph gives films of excellent detail and contrast - far superior to that by conventional equipment.

Limitations of Mammography

1. A certain amount of a fat is required to give contrast and the very dense glandular breast can be a diagnostic hazard.
2. Small breasts are not easy to project on to X-ray film. With the Senograph, it is possible to X-ray smaller breasts than with conventional equipment.

3. It is not possible with the Senograph to view the retro-mammary space in the supra-inferior view, because of the employment of compression of the breast between the cone and the base plate. It would appear possible that a minute lesion deep in the breast could be missed in this way, but a well positioned lateral view should obviate this; it is essential that great care is taken to position the breast correctly.

Frequency of Breast Screening Examination

Breast cancer is a complex condition with a highly variable natural history. In spite of work done on the growth rates of human tumours by Collins (23), and of breast tumours in particular by Ingleby (126), there is little agreement as to the optimum time interval between examinations to ensure early diagnosis.

In the mass screening programme, with matched controls, of the Health Insurance Plan of New York, Strax et al (14) did an annual review by clinical examination and mammography; Gerschon-Cohen (127), Egan (128) and Berger (124), all suggest a six-monthly mammogram. Gerschon-Cohen states that serial films at six-monthly intervals offer the best hope of detecting very small lesions, and that a repeat should be done at a three-month interval if there is a doubtful lesion.

Stevens (129) questions the need to repeat the examination annually as he detected no cancers at the second screening after one year. In this survey, three patients await biopsy at present, with abnormal thermograms and highly suspicious senograms, fourteen months after first screening date when all tests were normal.

I vary the recall time. If all findings are negative - on clinical, thermographic and senographic examination, an annual review is suggested. When only the thermogram is doubtful, the woman is recalled in six months; four asymptomatic cancers have been diagnosed on senography six, nine, fourteen and fifteen months after a positive thermogram but negative mammogram (TABLE 27).

When the X-ray is equivocal, an appointment is offered in three to four months time. I have found comparison of serial senograms to be most useful in picking up very small lesions and also in excluding a progressive lesion in a previously suspect area (ref. TABLE 23).

The fact that only three possible lesions (as yet unconfirmed histologically) have been found on annual review of 604 women, passed as negative by all three modalities a year previously, raises the question of the need for annual review in women considered to be negative at the initial screening.

As yet, this review is incomplete and it is too early to express an opinion on this aspect.

Some of my colleagues have expressed concern at the radiation to which these women are exposed. One elderly radiotherapist accused me of "causing, not diagnosing, breast cancer". Their doubts are mainly based on the paper by MacKenzie (130), who cites an increased incidence of carcinoma of the breast in women who had repeated chest X-rays over considerable periods of time while in sanatoria for treatment of pulmonary tuberculosis. The accumulated irradiation was as high as four thousand roentgens over a forty-six month period. This cannot be compared with the radiation from mammography, even when repeated at regular intervals - TABLE 29.

Samuel (63) states that there is no evidence whatsoever to suggest that the small doses of radiation used in mammography can have any relation to the malignant change which has been noted following radiation treatment (of the order of 2000 r) used many years ago for chronic mastitis. It is possible that when malignancy occurred in these breasts that it was the natural progression of an existing pre-cancerous dysplasia and had nothing to do with the radiation treatment.

Gerschon-Cohen (131) stated in 1965, and again with his colleagues Ingleby and Berger (127) in 1967, that there was no radiation risk in screening by mammography. This opinion has also been stated by Samuel (63), Egan (132), and by Martin (133).

The radiation from the Senograph is comparable to the dosage in other Units doing mammography and much less than in some - TABLE 29.

TABLE 29

Comparison of skin dose radiation in mammography

	Per Exposure
Egan (128)	2.4 to 2.8 r ad.
Witten (134)	3 r
+Strax et al (14)	5 r
Wolfe (135)	3.4 to 4.5 r
Griesbach (136)	3 r
Senograph (Phase III)	2.5 to 3 r

+During a recent discussion, Dr. Strax told me that his dose now, using the Senograph is 2 to 2.5 r.

The question of dose is constantly kept under review. It has been found possible to reduce the dose by the use of Industrex (Kodak)

film - without sacrificing the quality of the films, and this is being done now. The new Medichrome film (Agfa-Gavert) may enable even further reduction of dosage; as yet, it is not available in a suitable pack for use with the Senograph.

Accuracy of Mammography

The dense glandular breast is a diagnostic hazard for mammography, and the greatest accuracy occurs in the post-menopausal, atrophic, fatty breast. Egan et al (109) in their Comparative Mammography Study related the accuracy of mammography reports with the age of the woman and found mammography less reliable in the young, i.e., the woman with dense fibroglandular breasts in the reproductive years. The one false negative senogram report in this series was in a woman with dense glandular breasts with little fat and so no contrast; only 29.8% of the women in Phase III were post-menopausal.

As with thermography, the accuracy of mammography is well documented in clinical cancer - TABLE 30.

TABLE 30

Accuracy of Mammography in Clinical Cancer

Stewart, Gravelle & Apsimon (137)	92%
Gerschon-Cohen (127)	94%
Samuel (63)	94%
Egan (109)	88%
Nievelstein (138)	85 - 95%

Ochsner (139) compared the reliability of clinical diagnosis and mammography in cases with palpable findings - these were eighty eight percent and eighty nine percent respectively, but not always in the same cases. Saunders (140) and James (141) published similar figures.

It is interesting to compare these figures on the accuracy of mammography with the accuracy rates for standard X-ray procedures, as quoted by Samuel (63) - TABLE 31.

TABLE 31

Accuracy rates for various X-ray procedures	
Gastric ulcer	80 - 90%
Duodenal ulcer	83 - 94%
Carcinoma of colon	90%
Neurological lesions	64 - 92%

This would indicate that thermography and mammography are more accurate than many procedures which are generally acceptable to the medical profession, at a time when thermography (ref. TABLE 25 - accuracy 44.4% - 94%) and mammography (ref. TABLE 30 - accuracy 85% - 95%) are looked upon by some of my colleagues as "of no value and new fangled nonsense". No doubt, in time, they will appreciate its values. It is also important that they should accept its limitations, i.e., in the young women with dense active breasts. Thermography and mammography must not be looked upon as an alternative to biopsy, if the latter is indicated on clinical grounds. As detailed in TABLES 9 and 19, 48 biopsies were done on clinical grounds, irrespective of the findings on thermography and mammography.

TABLE 32

Pick up rates by clinical examination and mammography in Well Women

	Material	Age Group	Pick up per 1,000
Gerschon-Cohen (127)	1,120 examined at 6 monthly intervals over 10 yrs.	35 years +	3.5 at initial screening 8 in second year (36 in total over ten years)
Stevens (129)	1,223	40 years +	6.5
Wolfe (135)	3,891	75% post-menopausal	3.3
Friedman (142)	1,205	-	6
Witten (134)	5,014	-	1.6
Stevens (129) (Review of Literature)	10,000	-	3.1
Strax et al (14)	20,211 ten year survey	40 - 64	2.72 at initial screening

Several workers - Egan (132), Martin (133), Rogers (109), have published figures for pick up rates for occult cancer by mammography. These surveys are not strictly comparable, as age groupings, clinical findings and methods of mammography vary. More comparable, however, are the figures for Well Women as in TABLE 32 which confirm the wisdom of concentrating our limited resources on a high risk group of women, yielding a pick up rate of 21.6 per thousand.

To pick up impalpable cancers by mammography, it would appear essential that women will have to submit to more frequent biopsy, as a result of false positive mammograms - shown in TABLE 33.

TABLE 33

Percentage histologically proven cancers to positive mammograms in Well Women

Stevens	(129)	36.3
Wolfe	(135)	44.8
Strax	(143)	33.1
Witten	(134)	32
Stark - Phase II		32.1
- Phase III using Senograph		65.8

The results detailed in TABLE 33 confirm the superiority of the Senograph for soft tissue X-ray of the breast.

It is worthy of note that fifty percent of the false positive senograms in my series showed, on histological examination, lesions which some pathologists consider to be pre-malignant.

In a series of articles (144, 145, 146) published over 30 years ago, Muir gave an excellent description of the evolution of cancer of the mamma through all the stages from simple hyperplasia. He pointed out in 1934 that intra-duct cancer was frequently associated with epithelial hyperplasia at various stages of evolution, could be very chronic and be present for several years before becoming invasive.

The histology in these 50% of false positive senograms in my series is remarkedly similar to the microphotographs in Muir's article of 1941 and which he considered to be "approaching carcinoma".

These women will require very careful and prolonged follow-up. One of them (TABLE 20, Case No. 29), on review at six months after her biopsy, had a positive thermogram again and highly suspicious calcification on senography. The patient requested simple mastectomy

rather than a repeat biopsy and this showed a very small adenocarcinoma.

Of the thirty eight asymptomatic cancers in Phase II and III, eight were lobular in situ. Until relatively recently, lobular cancer was considered to be rare, Foote and Stewart (147) giving an incidence of 0.6% of all breast cancers in 1941. With the increasing use of mammography and greater attention being paid to the histological findings in asymptomatic cancer, higher frequencies are being reported, e.g., Newman (148) 10.2% half of which were in situ. Hutter et al (149) state that six percent of all breast cancers in their laboratory are lobular in situ, and draw attention to the frequency with which lobular in situ cancer is multifocal and/or bilateral, i.e., sixty four percent - this fact was also commented upon by Muir. There is ample evidence from the prospective studies of Hutter and Foote (150) and McDivitt (151) that a lobular in situ lesion is a pre-invasive form of cancer.

For these reasons, it is essential to maintain adequate follow-up of those patients. So far, only one patient with lobular in situ cancer has been found to have a bilateral lesion.

The incidence of bilateral lesions in the surveyed Well Women is 21%.

The factors, said to increase the risk of a bilateral lesion, are:-

1. family history

   Cady (152) reports a fifteen percent incidence of bilateral lesions in women with a family history of breast cancer.

2. Age at time of first breast cancer

   Berg and Robbins (153) have pointed out that women under fifty years when the first cancer is diagnosed, have a ten times increased risk of a contralateral lesion compared to the general population; the risk, if over fifty years, is twice that of general population.

3. Type of cancer

   When the first primary is multifocal, an anaplastic duct cancer (even poor prognosis does not mask the incidence of bilaterality), medullary, or lobular in type, there is a greater risk of a contralateral primary according to Berg and Robbins. Usetter et al (149) reported that 64% of their women with lobular in situ cancer had bilateral lesions.

In my series, these three factors occur in the patients in whom cancer was diagnosed as shown in TABLE 34.

TABLE 34

Incidence of factors increasing risk of a bilateral lesion (total number 38)	
Aged less than 50 years	60%
Family history	29%
Type of first primary Lobular in situ	21%
Multifocal (five breasts in three women, two of them having simultaneous bilateral lesions)	8%
Anaplastic	5.2%

This further emphasises the need for adequate long term follow-up, preferably using thermography and senography.

It has been shown that it is possible to diagnose breast cancer in a pre-clinical stage by the combined use of clinical examination, thermography and mammography.

Thermography with clinical examination appears to be adequate for the initial screening of unselected groups of women, reserving mammography for those with abnormal thermograms or clinical findings.

With the limited resources available at present, there is much to be said for concentrating on a high-risk group and employing all three modalities which are complementary, and employed as such provide a very thorough screen. Of the patients who had breast cancer in Phases I and II, only one (Mrs. S.J. ref. TABLE 11, Case No. 3) did not come into the high risk category.

In recent publications by Lowe and MacMahon et al (154, 155), the importance of age at first pregnancy in relation to risk of breast cancer is emphasised, the risk increasing with increasing age at first confinement. Data from their international collaborative study of this relationship suggest that the woman having a first pregnancy after her thirty fifth year may even be at greater risk than a nullipara.

The woman with a late first pregnancy, irrespective of her total parity, is now included in my high risk group, although on review of the records, they were in fact included previously, on the grounds of low parity.

I believe that these screening programmes should remain a hospital procedure, or at least be closely associated with a hospital in order that there is direct access to a surgeon, interested in this

work, and with sufficient beds and operating time to admit women for biopsy.

It is also essential that there is a suitable histology department. The average pathology department in a general hospital is not geared to "needle-in-the-haystack" histology, and it is no reflection on them that they do not have time to mount many blocks and cut numerous sections from each biopsy, as is required when dealing with very small lesions. The frozen section technique is not applicable to this type of biopsy in which there is frequently no macroscopic lesion.

Recently a report was published from Cardiff (156) on the use of clinical examination, thermography and mammography, using 70 mm. film and an Odelca Unit. They state: "Comparison of the diagnostic accuracy of these methods showed that neither thermography nor 70 mm. mammography has a useful place as an isolated screening procedure for breast cancer. In fact, we consider such a policy dangerous." I would agree that no one method is adequate as an <u>isolated</u> screening procedure. I would disagree, however, with their method of employing thermography. They describe how clinical examination was performed by a member of the surgical team, thermography performed by a technician and later the thermogram interpreted by a radiologist. I firmly believe that clinical examination and the thermographic findings must be

correlated at the time, for reasons previously stated; also a thermogram should not be treated like a chest X-ray but is more on a par with a barium meal. The opinion ought to be expressed by the screener, employing all the subtleties of the technique. It is a great disservice to thermography if diagnosis of breast conditions is attempted from thermogram films.

As to mammography, it is essential that films be of the highest quality. This is not possible with a 70 mm. Odelca Unit and automatic film processing - certainly such films cannot be compared with the detail and contrast of hand processed Crystallex films taken with the Senograph.

It is worthy of comment that the attitude of women to a breast screening clinic is quite different from that found in cervical cytology Well Women Clinics. During years of experience in the latter, and in gynaecological out-patients, where the majority of patients have cancer, I have seldom seen an emotional outburst from a patient. The attitude of women to breast screening came rather as a surprise. The demand for screening appointments is overwhelming and many are obviously nervous. During Phase II, when a second appointment was necessary for mammography, tears, hysterics and fainting were frequent occurrences.

I believe the reasons for this are:-

1. Breast cancer is so common that nearly everyone attending had personal knowledge of a victim.

2. Mastectomy is more mutilating than hysterectomy which, in fact, many women in their forties welcome.

3. The clinic attracted a number of hypochondriacs in the early days.

4. The attitude of one of our technicians did not help. In mistaken kindness, she was over compassionate to those women requiring mammography and this led some of them to fear the worst.

A matter of fact explanation is essential but it should be as a routine procedure.

During Phase III, the general attitude of the women participating is much calmer. While many are anxious to know the results, there have been no emotional scenes. This improvement is mainly due to the fact that all of them have thermography and senography done at the same appointment, instead of individuals being selected by thermography for further investigation, by mammography, the following day.

At a recent conference, I was asked if my selection of a high risk group would not lead to cancerphobia in this group. In fact, I have found that women are reassured that they are under regular observation each year.

Garrett (157) in Australia has raised the point that screening clinics could give a woman a false sense of security, and cites eleven women with breast cancer who became aware of a breast lump but delayed seeking medical advice until their next routine appointment some months later. This did not occur in any of the seven women who developed clinical cancers in this series. All promptly sought advice. In this country, I feel this would be the general rule in any woman sufficiently well motivated to attend voluntarily for routine screening.

It has been suggested that screening of Well Women for breast and cervical cancer could be combined, and in fact, this is being done at the Royal Marsden Hospital (158). I consider this is misplaced effort, and that these two procedures should be done independantly. My reasons are:

I. Breast cancer and cervical cancer have very different high risk groups.

(a) For the breast, the risk if highest in virgins, unmarried and nulliparous women. In the case of the cervix, those at greatest risk are the women with more than one sexual partner, whether promiscuous or a woman twice married. Whereas eighty six percent of our cervical cancer patients admit to more than one sexual partner, only six percent of the breast cancer patients give such a history.

(b) Breast cancer is uncommon in women under thirty-five years (three percent), whereas during 1969 and 1970, forty nine percent of the positive smears in this Department of Oncology occurred in women aged thirty five years or younger.

(c) The two cancers are more prevalent in different socio-economic groups.

II. The breast screening routine is much more time consuming than the taking of a cervical smear, and so the women are seen by appointment only for the former. In clinics doing only cervical smears, a briefer procedure, it is more practicable for the staff to deal with unexpected fluctuations in numbers.

III. As no major equipment is required for taking a cervical smear, such a clinic can be held in any convenient building. A proper breast screening clinic requires a temperature controlled unit with major expensive equipment and it would be uneconomic to use such a department for the taking of cervical smears.

It is not the purpose of this thesis to discuss the treatment of carcinoma of the breast. It is, however, of note that the majority of the asymptomatic cancers have been treated by simple mastectomy. This has several general advantages, in that it is not followed by lymphoedema of the arm or restriction of movement. As it is a simple

operation, the stay in hospital varies between seven and ten days and so the cost of treatment is considerably less than for a clinical cancer, which requires prolonged hospitalisation and probably deep X-ray therapy, long-term drug therapy and ablative surgery. This certainly will help to balance the cost of a screening programme. In the survey, it has cost two hundred and fifty pounds to find each case of breast cancer.

The end results of breast screening may never rival those for cervical screening, in that a positive smear indicates cellular or rather nuclear abnormalities and permits diagnosis at a stage of growth when cure is virtually one hundred percent.

In situ breast lesions depend for diagnosis - by thermography on an increased emission of heat, which is not always detectable, and - by mammography on micro calcification, which is known to occur in only 50 - 70% of instances.

There is the other point that cervical cancer is known to have a long-life history (159). A clinical cancer may not develop for up to ten to fifteen years after a positive smear is obtained. The rate of development of breast cancer is unknown as yet, but it is thought to be very much faster than that of the cervix, although Muir stated

that an intra duct cancer "may be present for several years before becoming invasive".

The ultimate test of the value of a screening procedure is improvement in the cure rate. Prolongation of survival time is not sufficient evidence of the efficacy of screening - when cancers are diagnosed in a pre-clinical stage, this automatically increases the survival time, even if the end result is unchanged.

While there is much evidence that early diagnosis improves the survival rates, only time can show if pre-clinical carcinoma of the breast is a curable disease. In my series, all the women in whom a diagnosis of pre-clinical cancer was made, remain fit and well - after an interval of eleven months to four years. It is planned to continue long-term follow-up for these patients.

The work of Strax, Shapiro and Venet (143) in the Health Insurance Plan of Greater New York, with their screened and control groups, should answer this question. Their recent publication reports that screening reduces the mortality from breast cancer, at least in the early years, the deaths in the screened (including women assigned to this group but who refused to take part) and control groups being 31 and 52 respectively. They state that these findings "provide grounds for cautious optimism for the long-term results".

The screening programmes, described in this thesis, continue. The routines of Phases II and III are progressing alongside each other, the former being used to select further high risk women. To date (June, 1971), 10,544 thermographic examinations have been done and 3,340 senograms.

CONCLUSIONS

1. Palpation of the breasts, by women themselves or even by clinicians, is not an efficient method of screening Well Women for breast cancer.
2. Clinical examination with thermography forms a worthwhile method of initial screening of Well Women in the diagnosis of abnormal breasts.
3. Thermography is inexpensive to perform although the capital outlay is great.
4. Considerable experience is required to interpret thermograms.
5. Thermography has no radiation hazard and can be repeated frequently; the fact that women have characteristic patterns is most helpful at repeat screening.
6. Thermography cannot distinguish benign from malignant conditions of the breast.
7. Thermography and mammography are required in conjunction for the diagnosis of pre-clinical malignancy.
8. With the senograph, films of excellent detail can be obtained quickly and easily; the senograph is superior to modified conventional equipment for mammography.
9. With a pre-clinical lesion, it is essential to X-ray the biopsy specimen; exhaustive search of the specimen by the

histologist is obligatory in view of the smallness of the lesions.

10. While resources are limited, there is much to be said for restricting the screening by all three procedures (clinical examination, thermography and senography) to high risk well women, selected by age, history, clinical and thermographic findings.

11. Cytology of nipple discharges is only of value when malignant cells are demonstrated; it should not be omitted, however, if a discharge is present.

12. The optimum interval between screening appointments for normal women is, as yet, uncertain.

13. With careful application of these methods, there is hope of improvement in the early diagnosis and cure rate of breast cancer.

14. The Pick up Rates for early cancer of the breast in this survey are as in TABLE 35.

TABLE 35

METHOD	Total Number	Age Group	Pick up per 1000
Clinical examination, with mammography in selected women	700	40 and over	1.4
Clinical examination and thermography with mammography in selected women	3684	21 to 74	2.4
	2664	35 to 74	3.4
Clinical examination, thermography and senography in high risk women	1017	34 to 72	21.6

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THE SCREENING OF WELL WOMEN FOR BREAST CANCER

by
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SUMMARY

This thesis is based on work done in screening Well Women for the detection of early breast cancer during the period September, 1967, to June, 1971.

The work was undertaken because of the high incidence of breast cancer, and the fact that there has been little improvement in survival rates for breast cancer in the past fifty years - in spite of developments in treatment. It has been shown by others that the smaller the neoplasm at the time of initial treatment the greater the chance of cure.

The aim of the project is to diagnose breast cancer before there is a palpable mass.

The methods used are

(1) history
(2) clinical examination
(3) cytology of nipple discharge, if relevant
(4) thermography using an Aga Thermovision
(5) soft tissue X-ray
    (a) at first by conventional X-ray equipment (mammography)
    and (b) from December, 1969, by the Senograph (senography)

Medical thermography and its application to breast lesions is described with appropriate references to the literature.

The technique of breast thermography used is detailed. The interpretation of the thermograms, and the factors influencing this, is discussed and illustrated.

The history of mammography is reviewed.

The X-ray signs of malignancy are enumerated and described at length. Illustrations of the technique of using the Senograph and a series of representative films of senograms are presented, with comments. Particular reference is made to difficulties in interpretation of senograms, in spite of the latter being superior to films taken by conventional equipment.

A description is given of the Unit, designed for this work, and the organisation of the clinics.

The work falls into three phases

Phase I

consisted of seven hundred women, aged forty to sixty-three, who were examined clinically. On account of palpable findings, fifteen per cent were referred for mammography.

Phase II

comprised 3,684 unselected women, examined clinically and by thermography. Of these, 10.9% were referred for mammography on account of palpable findings and/or abnormal thermograms.

Phase III

consisted of 1,017 highly selected women, considered to be at high risk of breast cancer. The high risk factors are enumerated and discussed in depth.

During Phase III, all women were examined by all three methods - clinical examination, thermography and senography.

The Biopsy

The importance of ensuring that, in the absence of a palpable mass, the correct area has been removed at biopsy is stressed and the technique is described.

Detailed results are given in tabular form.

The pick-up rates are as shown below

Method	Total number	Age group	Pick-up per 1,000
Clinical examination, with mammography in selected women	700	40 and over	1.4
Clinical examination and thermography, with mammography in selected women	3,684	21 to 74	2.4
	(2,664	35 to 74	3.4)
Clinical examination, thermography and senography in high-risk women	1,017	34 to 72	21.6

The following points are discussed

(1) The accuracy of thermography and mammography (including senography) with the advantages and disadvantages of these investigations

(2) The Question of false positive and false negative results with suggestions for improvement

(3) The histology of the biopsy with special attention to that present in false positive results

(4) The frequency of breast screening with particular reference to irradiation

(5) The value of well women screening for breast cancer, especially when restricted to women in a high-risk group

(6) The cost in time of trained personnel and capital outlay.

The thesis ends by listing thirteen conclusions evolved during the course of this work and which indicate the merits of clinical, thermographic and senographic examination in the screening of well women for breast cancer.